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SOME EXPERIENCES WITH INTRACARDIAC SURGERY

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IT HAS become traditional in this Society for the President in his address to speak on a scientific subject of particular interest to himself. I shall continue this tradition by discussing our experiences in our first 100 open heart operations employing extracorporeal circulation.

One of the great privileges of being a contemporary vascular surgeon has been the opportunity to live through the developmental period of open cardiac surgery. Time does not permit me to give credit to the many pioneers of this field, most of whom you know as members of this Society, but perhaps we should not omit pointing again to the great role played by the experimental laboratory in developing this field. Without question, the vast body of young men from all over the world who have had access to these laboratories are the ones to whom we must give the most credit for pushing this field forward so rapidly.

Although we must acknowledge that hypothermia has been an important aid in open cardiac surgery, it is becoming apparent that its usefulness is gradually being supplanted by the success of extracorporeal circulation. Hypothermia may finally be used only as an aid in the repair of certain valvular defects and as a metabolic adjunct in a variety of surgical procedures. As our understanding of pump-oxygenator systems becomes wider, their efficiency and the security they provide will surely obviate the necessity for haste during delicate intracardiac operations.

The variety of pump-oxygenators now available only serves to remind us of the value of careful research in any field, for on close scrutiny one finds that the fundamental facts established by a few pioneers govern the basic construction

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of them all. During the past 3 years our unit has subjected a number of pump-oxygenator systems to laboratory and clinical evaluation. Animal experiments convinced us that those which rely on passing bubbles of oxygen through blood, although inherently simpler, are fraught with more hazards than those which oxygenate blood on films. It is a curious fact, however, that it is difficult to find much difference in the effect of these systems on the blood itself, but this may be due to our lack of the proper techniques for finding them. It was very clear to us that the low flow principle would not be satisfactory; neither was interference with the normal venous pressure relationships.

The inevitable conclusion we all have come to is that the closer our extracorporeal circulation approximates the normal physiologic status of the patient the better off he is. High flows are required to do this. It is our opinion that at present film oxygenators provide high flows more safely than the bubble oxygenators. We have been using two different filming systems, one which employs filming on disposable polyethylene bags and the other the disc-type oxygenator developed by Melrose. We are currently modifying the Melrose oxygenator to make it autoclavable; electively the discs may be used as disposable units. It is possible that in the near future the membrane oxygenator will occupy a firm position. This depends upon whether or not satisfactory membranes will be available. Thus far our laboratory experience with the 0.8 mil polyethylene membrane has shown that although the transmission of oxygen is satisfactory carbon dioxide is not. It is possible that to make such an oxygenator maximally efficient two types of membranes may be required, one for oxygenation and another for removing carbon dioxide.

Our studies of the blood chemistry also indicate the desirability of maintaining high perfusion rates. The mean pH values 2 hours postoperatively showed a reduction of only 0.08, and at 6 hours they had approached normal. The mean sodium, potassium, and chloride determinations fell slightly postoperatively, but these differences were probably due to dilution with intravenous fluids and water retention. Lactate determinations showed a mean preoperative value of 26 mg. per cent and a postoperative value of 36 mg. per cent. It should be remembered that approximately 88 per cent of the patient's blood volume after perfusion is from donor blood, which may have a high lactate content.

One of the most important factors in the future of this whole field is the supply of blood. Up to the moment local blood banks have extended themselves to meet the needs of this field. In some cities it is all one blood bank can do to supply the requisite number of donors to maintain one unit engaged in an active program employing extracorporeal circulation. Reducing this to numerical figures, an average perfusion requires that eight 500 c.c. units of heparinized blood be available and an additional 5 units for use in the postoperative period. The Irwin Memorial Blood Bank in San Francisco processes 150 units of blood per day. Thus one case requiring extracorporeal circulation consumes 9 per cent of the total daily effort of the bank. We have frequently done two operations on one day, doubling the requirement.

We might well look to means of reducing our requirements by being more meticulous in operative hemostasis, but a reduction in the priming volume of our machines should be our most serious goal. At present this varies between 3,000 and 5,000 c.c. It should be possible to reduce it to 1,000 c.c.

We had thought that postoperative bleeding problems caused by interference with the coagulation mechanism would be frequent. Fortunately, this has not been true generally, although there are occasional instances. As might be expected, they are more apt to occur following long perfusions, particularly if a substantial quantity of blood is aspirated from the heart during the repair. In my experience excessive bleeding postoperatively is more apt to occur as a result of some inadequacy of the operative procedure than from a failure of the coagulation mechanism. Protamine titration of the blood of heparinized patients may not always be necessary, but it is useful in many instances.

Postoperative bleeding on a few occasions has caused pericardial tamponade despite liberal fenestration of the pericardium, or hemothorax has resulted from pocketing of blood in clots where it was inaccessible to the drainage tubes. Whenever we recognize or suspect that tamponade or pulmonary insufficiency is due to collected blood we return the patient to the operating room and re-explore the operative area. The median sternotomy incision, fortunately, is easy to reopen and resuture in such circumstances. We have never regretted a re-exploration, but unfortunately a number of our postoperative deaths can be blamed on our failure to recognize these complications until it was too late.

Postoperative digitalization of the patient has been done whenever there has been some reason to expect borderline heart failure, or when it develops. This is frequently a hard decision to make, but when there has been any question as to whether it might be of benefit, except in the presence of heart block, we have usually proceeded at once.

There is undoubtedly much to learn about the physiology of elective cardiac arrest, but we believe that it is preferable to use it in most interventricular repairs. Experience has shown that certain precautions must be observed, however. We have used the dilution of 1 c.c. of 25 per cent solution of potassium citrate in 10 c.c. heparinized oxygenated blood, as suggested by Melrose. The mixture should be injected rapidly into the base of the aorta just after it is cross-clamped and after the heart has been emptied by having the patient on total bypass. No more than is required to stop the heart is injected, and the ventriculotomy should be made without delay to prevent distention of the heart. More often an exploratory ventriculotomy is done before stopping the heart. Although it is possible to arrest the heart, with recovery, for prolonged periods of time, we have found that fewer arrhythmias will occur if a 30-minute period is not exceeded. Frequently the repair is tested by allowing the heart to restart when the repair is completed and before closing the ventriculotomy. One of the most important aspects of elective arrest is the avoidance of left ventricular distention, for when this has occurred weak heart contraction will result. To repeat, protection against distention is gained by stopping the heart only after

it has been emptied on total bypass or after the ventricle has been opened, rapid injection of the potassium mixture, and during the recovery phase by manually compressing the heart if it tends to dilate.

It has been stated that one should not produce elective cardiac arrest in the adult because of the difficulty of restarting such a heart after the repair has been completed. We have seen this occur in patients with mitral insufficiency, but not those with ventricular septal defects. A recent experience in the second patient from whom we were able to remove successfully a large myxoma of the left atrium demonstrated the need for an unusually large flow to restart such a heart. The heart was stopped for 16 minutes while the tumor was removed. The clamp was then released from the aorta to permit coronary perfusion, but, despite a 4.5 L. flow and a line pressure of 175 mm. Hg in a 72 Kg. man, the heart remained flaccid and poorly oxygenated. It was only after the line pressure was raised to 400 mm. Hg with a flow of 6.5 L. per minute that cardiac action returned. We interpret this as meaning that some adults have poor coronary circulation and therefore require high perfusion pressures and flow to remove the potassium and metabolic products.

Similarly, it has been our experience that flow rates which by calculation would seem to be adequate to maintain a satisfactory blood pressure occasionally are not. This is undoubtedly related to differences in peripheral resistance, venous pooling, and other alterations in circulatory physiology during heart-lung bypass, as yet poorly understood.

In our first 10 patients operative exposure was obtained through transverse thoracotomy. This we found gave good access to all the important structures, but frequently the procedures involving the superior mediastinum had to be performed under the ledge of the retracted thoracic cage. There was also distortion of the mediastinal structures caused by the longitudinal stretch of this type of incision. Our main reason for abandoning this incision, however, for most intracardiac procedures, came from observations on postoperative respiratory function. Patients who have had a bilateral thoracotomy do not ventilate easily or well because of the extensive and painful nature of the wound. Approximately a year ago we began using the median sternotomy as our routine incision and find it easier, faster, and much less painful than the bilateral incision. The left internal mammary artery is cannulated for continuous arterial blood pressure determinations. The central venous pressure is monitored in the inferior vena cava via the left saphenous vein; the same incision is used for the retrograde common femoral arterial perfusion.

The approach has been criticized as being poor for the visualization of persistent left superior vena cava. Nothing could be further from the truth, for one needs only to retract the left atrium downward to bring it into view, and the dissection required to pass a tape around it is not complicated. A more just criticism may be made of it for the control of a patent ductus, particularly if the pulmonary artery and heart are grossly enlarged. Under such circumstances an additional transverse incision may be required. It is possible to expose the ductus intrapericardially by dissecting down the superior margin of the pulmonary artery.

There is still question as to whether extracorporeal circulation should be used for the correction of some cardiac abnormalities, but as experience is gained more lesions are added to the growing list. For example, last year, after completing the repair of 40 atrial septal defects using external suturing techniques, without operative fatality, we became convinced that the frequency of associated abnormalities was so high that it made us wish for more time to examine the interior of the heart and more security in the type of repair required. We have never believed that hypothermia would allow us this time and security in all cases. We now routinely employ extracorporeal circulation for the repair of atrial septal defects and have done the last 20 consecutive cases without fatality.

It is hard to justify nonoperative treatment for the majority of ventricular septal defects. Those patients who have an uncomplicated defect may be operated upon with a mortality rate of less than 5 per cent. Those who have defects associated with pulmonary hypertension have a higher risk but often require repair more urgently. It is my belief that there are a few patients with marked pulmonary hypertension in whom this aspect of their disease will continue progressively or remain as it was, despite closure of an interventricular defect.

Most children who have lived beyond early childhood with tetralogy of Fallot should now have the definitive operation of complete repair. There will always be a sound place for systemic-pulmonary artery anastomoses where the defects in the right side of the heart or outflow tract are beyond correction. A successful operation for the complete correction of this abnormality is one of the most gratifying of operations, for removal of the infundibular obstruction and closure of the defect allow the heart to adjust to near-normal function. Our surgical difficulties with this defect have come mainly from reoperating upon patients who have had one or two previous procedures. The exposure and dissection required to cope with the artificial ductus add greatly to the magnitude of the operation and postoperative care. In fact, this experience has led us to believe that the palliative shunting procedure should rarely be used when there is a reasonable prospect of being able to do an open operation. The other principal cause of operative death has come from being unable to fashion a proper right ventricular or pulmonary artery outflow tract. Undoubtedly, we should have resorted more frequently to the use of plastic materials to accomplish this.

One patient, aged 13, with tetralogy had a failure of the repair during the immediate postoperative period. Massive flooding of the lungs, with a shunt of 18 L., and heart failure occurred. This seemed far greater than one sees in a pure ventricular septal defect of the same size, suggesting that in the latter nature has provided a protective mechanism in the lungs in the form of a resistance to flow which in a sense prevents a huge shunt. After 4 weeks of rather desperate care we reoperated and found that the sponge prosthesis had become separated from one side. It was removed, and an excellent direct suture was possible due to the fibrous reaction resulting from the previous operation. His recovery was complicated by a massive hemothorax and hemopericardium, which when relieved resulted in complete recovery.

Another complete failure occurred in an 11-year-old girl with a large interventricular septal defect. In this instance we reoperated successfully after 2 weeks and found that the tissues were easier to separate than they had been at 4 weeks, and there were fewer adhesions with an established blood supply to cause postoperative bleeding.

Our attitude toward the treatment of congenital aortic and pulmonic stenosis has undergone some change in the past 2 years. We continue to use hypothermia as an aid in the treatment of valvular pulmonic stenosis in infancy and early childhood but now routinely use extracorporeal circulation for grown children and adults with this abnormality. When there has been an associated severe work-hypertrophy causing infundibular stenosis in the right ventricle, a portion of the muscle has been resected through a ventriculotomy incision. No doubt, in many instances this hypertrophy will regress in time after the valvular stenosis has been relieved, but it is probably also true that this acquired type of infundibular stenosis may reach the point where it cannot relieve itself, resulting in a form of suicidal heart disease.

The relief of congenital aortic stenosis may require a precise, unhurried operation on the valve or subaortic area, and for this reason we employ extracorporeal circulation and elective cardiac arrest in operations upon this condition.

It has been said that we will soon be utilizing the open operation with the aid of extracorporeal circulation for mitral stenosis. This may well be true, but the results of closed operation continue to be excellent, with a low operative mortality rate, and therefore the possible gain from having visual access is not great. During the past 3 years we have abandoned the knife as a means of starting a split at the commissure and now routinely, in difficult cases, fracture the valve from the transventricular approach with a thin valvulotome capable of opening two flat blades to a diameter of 6 cm. It is guided into the stenotic orifice with the right index finger in the left atrium, then gradually opened. One can usually get a nearly complete separation of the commissures with this technique, and, although there is the real possibility that serious regurgitation might result, this has not occurred as yet.

We have had a limited and unrewarding experience in the treatment of mitral insufficiency. It is unfortunate that the greatest number of patients who are in serious difficulty with this disease have heavily calcified or very fibrotic valves which require more than a plastic repair of one commissure. We shall have to rely upon plastic materials which can become a part of the moving valve for the vast majority of such patients; the recent contributions of Lillehei and his group are encouraging in this respect.

Of all the aspects of intracardiac surgery the postoperative management is the most important. The patient is weighed in the operating room preoperatively for comparison with the postoperative weight; this gives one a fairly good appraisal of where one stands relative to blood volume, and any gross deficit is corrected. Usually we have tried to stay approximately even, although it is often obvious that a positive blood balance is required. During the first 48

hours we endeavor to replace, steadily, what is lost in chest drainage. Fluids are given at a rate of 400 ml. per square meter the first 24 hours, and 800 ml. per square meter thereafter. When any acidosis is detectable one unit of molar sodium lactate is given. Greatest care is given to maintaining an adequate respiratory exchange, for these patients can slip into respiratory acidosis very quickly. Directly after operation, and while the patient is being established in the recovery unit, supported respirations are maintained by the anesthetist until the patient no longer will tolerate the intratracheal tube. Thereafter, an oxygen tent is used. Whenever there is any question about respiratory depression, the nurse is instructed to require the patient to take deep breaths, at times through an oxygen mask. There are occasions when tracheotomy and mechanically assisted respirations are necessary.

It can be said truthfully that one has to pass through a generous experience in a new field before many of the simple lessons are learned. Certainly, as we gained experience our results improved.

I would like to make it quite clear that intracardiac surgery of this type is a team effort in which equal and great responsibilities are shared by each member of the group. The preoperative evaluation, the physiology of perfusion, and the management of postoperative care assume equal importance with the operative procedure. In this respect I wish to pay particular tribute to my associates, John Osborn and Denis Melrose, who have contributed so generously of their time and effort to make this field a safe and fruitful one.

STUDIES IN CORONARY ANGIOGRAPHY

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THE key to the interpretation of the pathologic anatomy in peripheral arteriosclerosis obliterans is the arteriogram. Without arteriography it would not be possible to select the patient with segmental disease as candidates for direct arterial operations, such as bypass or endarterectomy procedures. Similarly, in coronary arterial occlusive disease it is expected that coronary angiography will aid (1) in evaluating the extent of occlusive disease in patient with coronary insufficiency and (2) in providing a sound basis for the use of existing surgical procedures or for the development of new operations designed to alleviate coronary insufficiency. Unfortunately, our impression of the relative incidence of segmental versus diffuse coronary occlusive disease is based upon autopsy material from patients dying at the end of a long course of coronary disease or from unselected autopsy material including incidental findings of asymptomatic coronary occlusive disease.[1] This would be analogous to accepting material from gangrenous amputated limbs or autopsy material from unselected series to decide on the incidence of segmental versus diffuse femoral arteriosclerosis obliterans. Just as the correct answer has been derived from femoral arteriography in patients with claudication, it is hoped that the true incidence of segmental coronary disease will be derived by coronary angiography in the patient with angina.

It is also paradoxical that the operative procedures developed in the past two decades to relieve coronary insufficiency are based mainly upon the protective action of such operations in preventing ventricular fibrillation after coronary arterial occlusion in an otherwise healthy dog. This does not take into account what the true nature of the underlying pathologic anatomy may be in the patient with angina.

Unlike the extremity with arteriosclerosis obliterans, the heart is a vital organ with a rhythmic function. Arrythmias, fibrillation, and arrest are potential hazards of coronary angiography. Thus it is of extreme importance to test the variables of technique to provide maximum safety from arrythmias or permanent damage and yet achieve adequate coronary visualization. Since the pioneer work of Grossman,[4] there have been other studies of coronary angiography in dogs by various techniques.[2, 7, 10-12] More recently Collho,[3] Helmsworth,[5] Hoyos,[6] Lehman,[8] Radner,[13] and Thal[14] have carried out successful attempts to visualize the coronary arteries in the living human patient by different methods. This study was designed to evaluate systematically the

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many variables in coronary angiography on dogs with myocardial infarcts secondary to ligation of the left anterior descending coronary artery. Our goal was to develop a method that gave adequate visualization consistently without any apparent ill effects.

MATERIALS AND METHODS

Multiple studies were carried out in a colony of 46 previously healthy mongrel dogs weighing between 10 and 20 Kg. The usual sequence of events was to do a base line coronary angiogram. One week later the left anterior descending coronary artery was ligated. Two to six weeks postligation the coronary angiogram was repeated and the dog was sacrificed and autopsied 48 hours later.

Variables evaluated were as follows.

A. For better contrast visualization.—A number of contrast media in different concentrations were used. Hand injection was compared with the automatic injector. The rate and pressure of the automatic injector were varied. The optimum location of the intra-arterial catheter was evaluated. The use of temporary acetylcholine arrest immediately preceding the contrast injection was studied. With acetylcholine arrest* the detailed visualization in using the Schönander multiple exposure x-ray machine was compared with a single tabletop exposure x-ray film.

Technique currently considered most satisfactory: The anesthetized dog (intravenous Nembutal, 1.0 c.c. per 5.0 Kg.) is maintained on a slow intravenous drip of normal saline through a polyethylene catheter inserted in the jugular vein. The common carotid artery on the same side is isolated and occluded with a loop of silk suture after a No. 8 woven intra-arterial catheter is threaded retrograde to a distance of about 15 cm. If the catheter impinges on the aortic valves, a characteristic click is felt; the catheter is then withdrawn 1 to 2 cm. If no click occurs, the catheter is presumably in the descending portion of the aortic arch.

Under fluoroscopic control the tip of the catheter is placed at the junction of the ascending aorta and the brachiocephalic artery. This is facilitated by introducing small bursts of 50 per cent Hypaque and observing the pulse wave and direction of blood flow. The catheter is firmly secured to the syringe (containing 25 to 30 c.c. of radiopaque media) of the automatic injector. The dog is strapped in the right posterior oblique position. The technique employed is 100 Ma., 0.1 second (10 MaS), and 75 to 80 KvP using an 8-1 grid.

A preinjection base-line ECG is taken. While the tracing is observed, a bolus of 5 to 8 mg. of acetylcholine is injected rapidly into the vein and flushed through with normal saline. Three seconds after asystole is identified, the firing mechanism of the automatic injector is released (Fig. 1). When the plunger is within 5 c.c. of completion, the exposure is made. ECG monitoring continues until the preinjection base line level is obtained. The carotid arteriotomy is repaired with arterial silk.

B. Methods for Evaluating Myocardial Damage.—ECG tracings were taken before, during, and at periodic intervals after each procedure. Serum transaminase levels were determined before and after each procedure. Detailed histologic examinations of the heart were carried out at necropsy and particular attention was paid to any evidence of fresh damage (due to the last angiography) superimposed on the old myocardial infarcts.

RESULTS

For optimum visualization 50 per cent Hypaque proved to be superior to 90 per cent Hypaque, 70 per cent Urokon, 80 per cent Cardiografin, and 35 and 70 per cent Diodrast (Fig. 2). Thorotrast provided equally good visualization as the Hypaque. However, the use of Thorotrast would be restricted

*This was suggested by a discussant from France at the October, 1957, meeting of the International Society of Angiology. We regret all efforts to trace this physician to give him proper credit have failed.

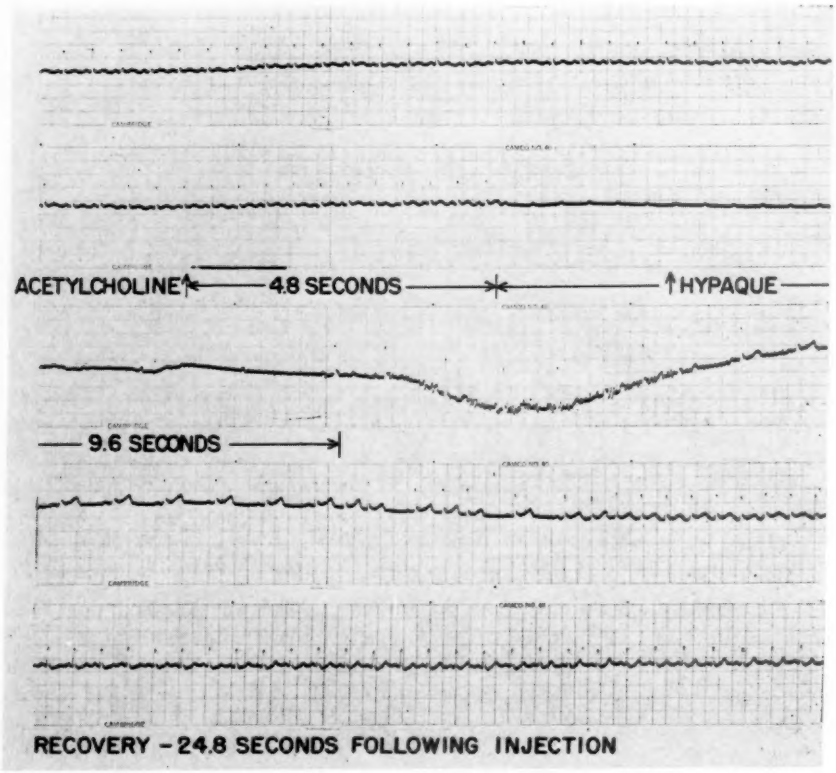

Fig. 1.—A preligation electrocardiogram showing acetylcholine (4 mg.) cardiac arrest in Dog 14 NC (weight 10.0 Kg.) for a period of 9.6 seconds. Approximately 3 seconds after the initial asystole, 30 c.c. of 50 per cent Hypaque was injected. Full recovery to normal rate and rhythm appeared 24.8 seconds following injection of acetylcholine.

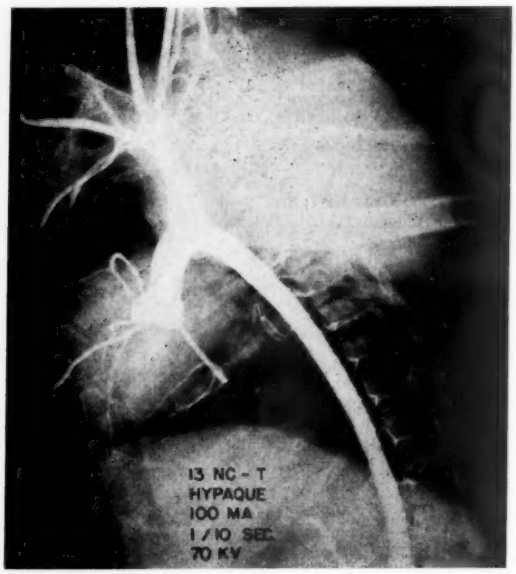

Fig. 2.—A preligation coronary angiogram taken with the single exposure tabletop technique (T) using 30 c.c. of 50 per cent Hypaque and acetylcholine cardiac arrest.

particularly in younger patients to obviate the possible development of neoplasms of the reticuloendothelial system. Histologic studies have also revealed Thorotrast foreign-body granulomata in the myocardium; such granulomata were not present when Hypaque was used (Fig. 3). Higher concentrations of Hypaque were found to cause a greater degree of electrocardiographic disturbance and yet did not provide any better visualization of the coronary arteries. The automatic injector was found to be superior to hand injections and a pressure of 120 pounds per inch^2 over a 4-second period provided consistently adequate coronary visualization. The best location for the tip of the intra-arterial catheter was at the junction of the brachiocephalic artery and the ascending aorta; when the tip of the catheter was moved down to the level of the sinuses of Valsalva, there was, on occasion, filling of one coronary artery only.

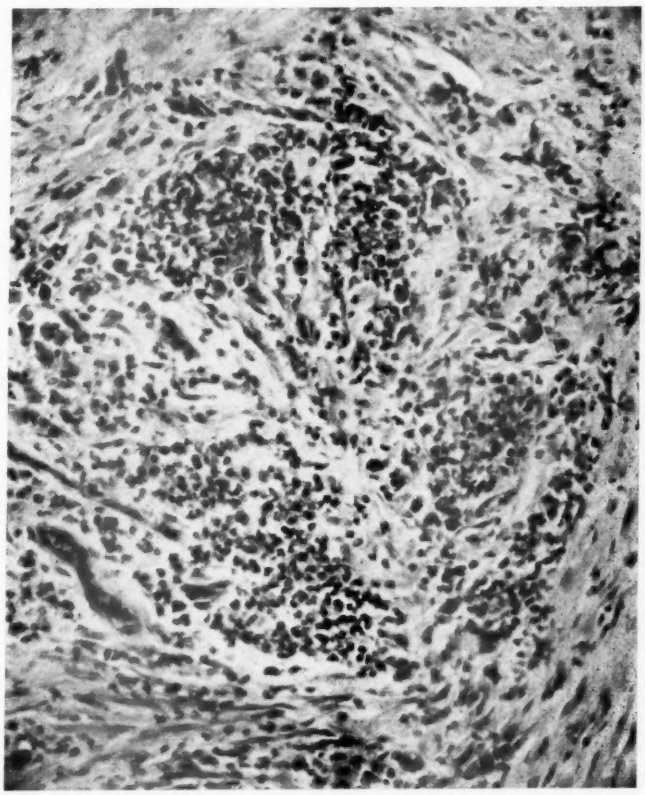

Fig. 3.—A Thorotrast granuloma in an old myocardial scar near the point of ligation of a coronary artery. The chronic inflammatory cellular infiltrate consists of swirls of epithelioid cells, macrophages, plasma cells, small and large lymphocytes, and occasional foreign-body giant cells. Aggregates of Thorotrast particles situated intra- and extracellularly are not seen at this magnification. (Masson, ×250.)

Acetylcholine arrest has been the most rewarding addition to the technique. Four to 8 mg. of acetylcholine intravenously consistently produced a temporary asystole lasting approximately 5 to 15 seconds. During this period of asystole, the automatic injector was set off, and the resultant visualization of the coronary vessels has been unexcelled in our experience (Fig. 2). Contrary to

our theoretical expectations, the acetylcholine arrest did not cause any residual damage even in the postligation dogs as judged by the ECG tracings, the serum transaminase levels, and the histologic studies. With or without acetylcholine arrest, coronary angiography caused some temporary ECG changes (Fig. 4) with reversion to a normal preinjection tracing within 3 to 6 minutes. When the same amount of acetylcholine was used intravenously without concommitant coronary angiography, the asystole also lasted between 5 and 15 seconds with reversion to a normal prearrest tracing within 3 to 5 minutes (Fig. 5). There were no deaths attributable to the use of acetylcholine arrest, and there was no

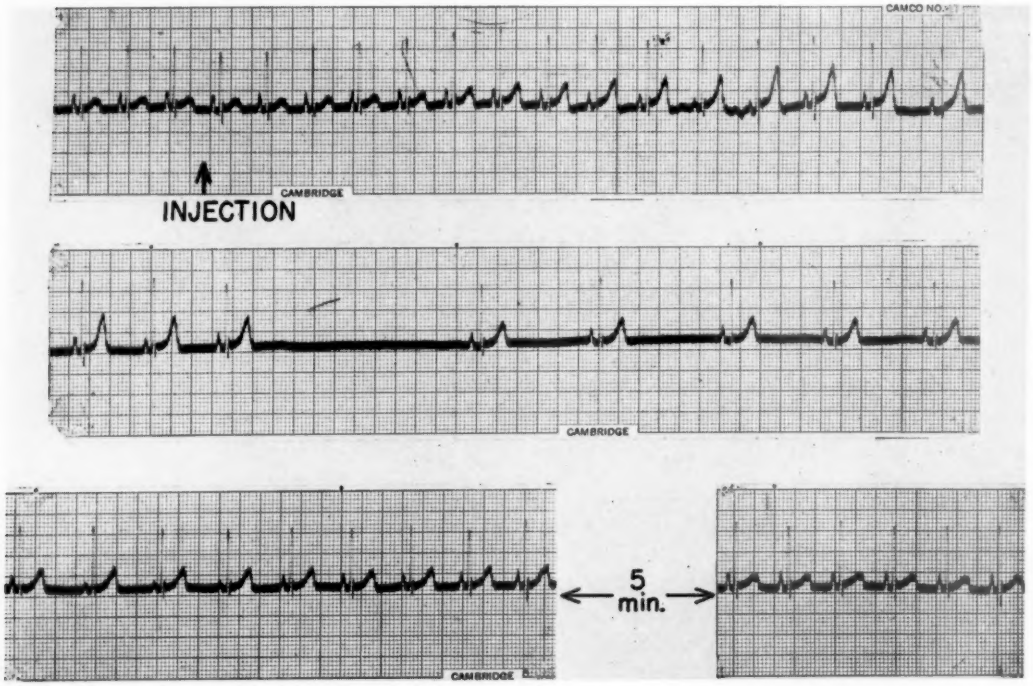

Fig. 4.—A preligation electrocardiogram showing injection of 30 c.c. of 50 per cent Hypaque *without* acetylcholine arrest. Marked S-T wave changes are noted temporarily with reversion to preinjection tracing within 5 minutes.

difference in the effect of the drug between the preligation and postligation groups (Table I). The acetylcholine arrest also permitted the use of single x-ray exposure films with a bucky grid for greater detail; the exposure was coordinated with the onset of asystole as monitored by the ECG tracing. With experience the single exposure film has proved to be superior to the Schönander multiple exposure technique. The coronary visualization is superior and leaves little further to be desired (Figs. 2 and 6). Also the amount of exposure to radiation of personnel and cost of equipment is reduced drastically. This

TABLE I. CORONARY ANGIOGRAPHY ACETYLCHOLINE INDUCED CARDIAC ARREST

	PRELIGATION (18)	POST-LIGATION (14)	ALL (32)
Injection to asystole	3.56 sec.	4.73 sec.	4.07 sec.
Asystole to ventricular contraction	8.59	8.26	8.48
Recovery	36.40	36.78	36.28

technique brings coronary angiography within the realm of departments of radiology or experimental surgery not equipped with a Schönander or similar unit.

Whereas ligation of the left anterior descending coronary artery produced a significant elevation in serum transaminase level, no change in the latter was noted following coronary angiography pre- or postligation and with or without acetylcholine arrest. Histologic studies carried out on the dogs sacrificed 48 hours after postligation coronary angiograms failed to reveal any evidence of acute morphologic changes superimposed on the old myocardial infarcts (Fig. 7).

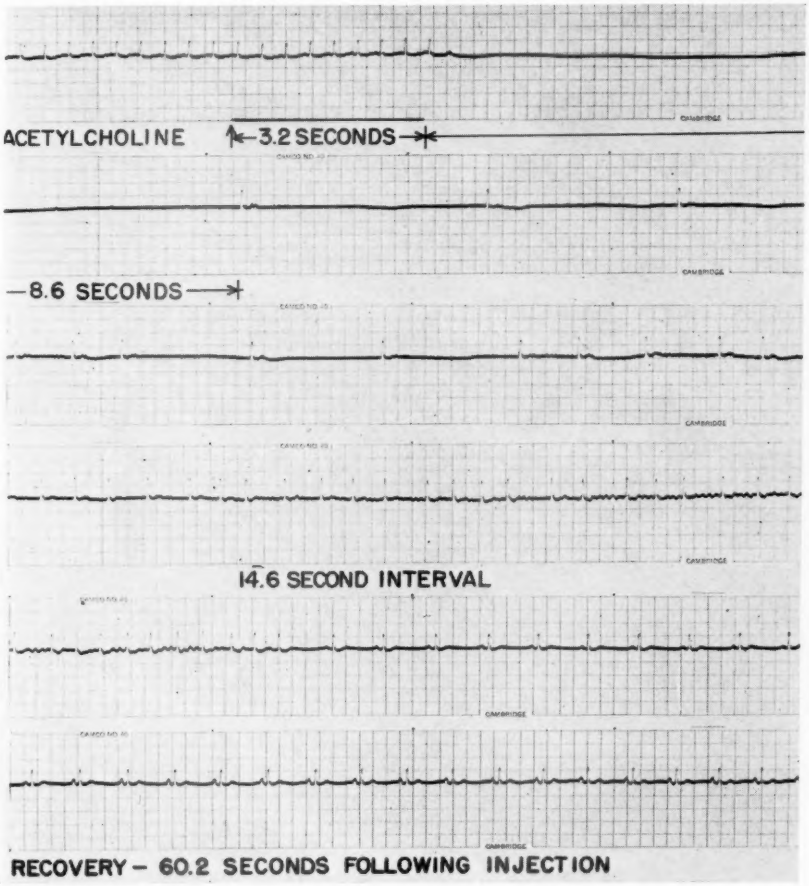

Fig. 5.—A preligation electrocardiogram showing acetylcholine (4 mg.) cardiac arrest in Dog 14 NC (weight 10.0 Kg.) for a period of 8.6 seconds. Full recovery to normal rate and rhythm appeared one minute following injection. No coronary angiograms were taken.

COMMENT

In the dog with a coronary arterial occlusion, coronary angiography proved to be a safe procedure even with the use of temporary acetylcholine arrest. The latter provided superb visualization of the coronary arteries consistently using the simplest radiographic equipment. This is in contrast to the method suggested by Miller[11] using potassium arrest and a pump-oxygenator resulting in the death or 5 of 10 dogs.

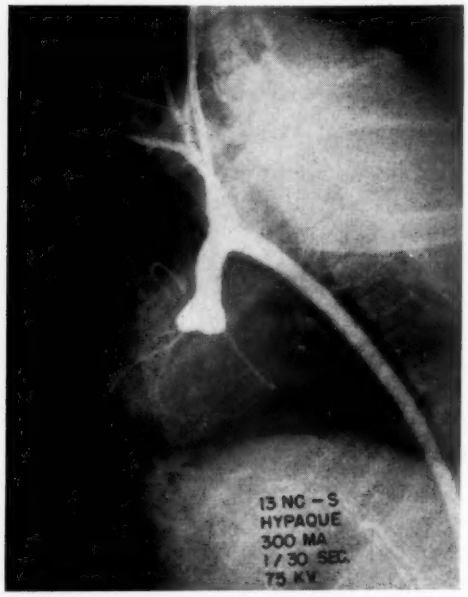

Fig. 6.—A preligation coronary angiogram taken with the Schönander (S) unit using 30 c.c. of 50 per cent Hypaque and acetylcholine cardiac arrest. A loss of detail is observed as compared to a similar angiogram done with the single exposure tabletop technique (T). (See Fig. 2.)

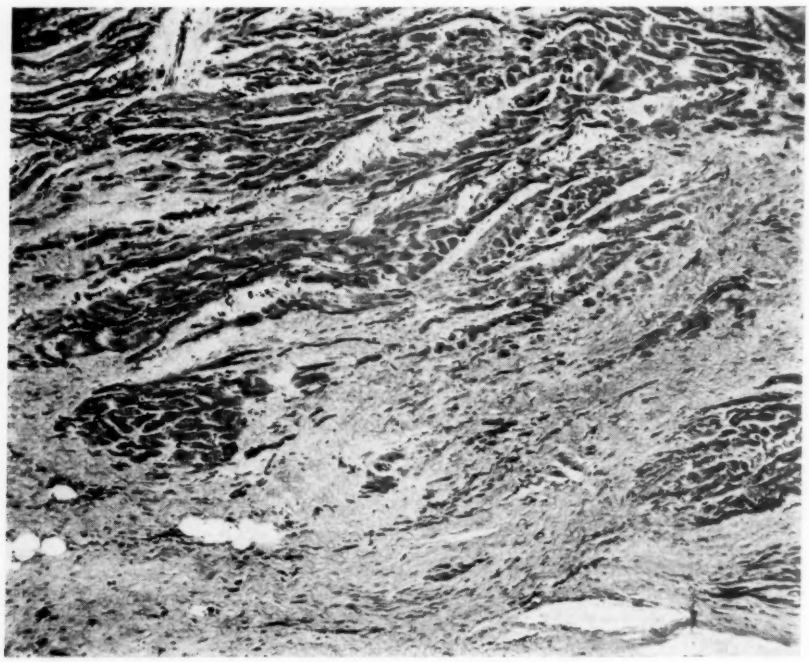

Fig. 7.—A photomicrograph of a portion of the infarcted myocardial wall showing scar formation in a dog 4 weeks following ligation of the left anterior descending coronary artery. There is no indication of toxic changes induced by the recent use of radiopaque materials or intravenous acetylcholine. (Masson, ×35.)

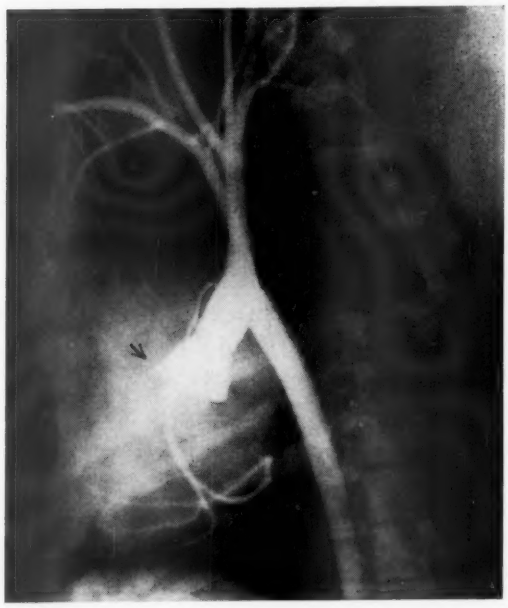

Fig. 8.—A postligation coronary angiogram using 30 c.c. of 50 per cent Hypaque and acetylcholine cardiac arrest in which the point of ligation of the left anterior descending coronary artery is clearly visualized (arrow).

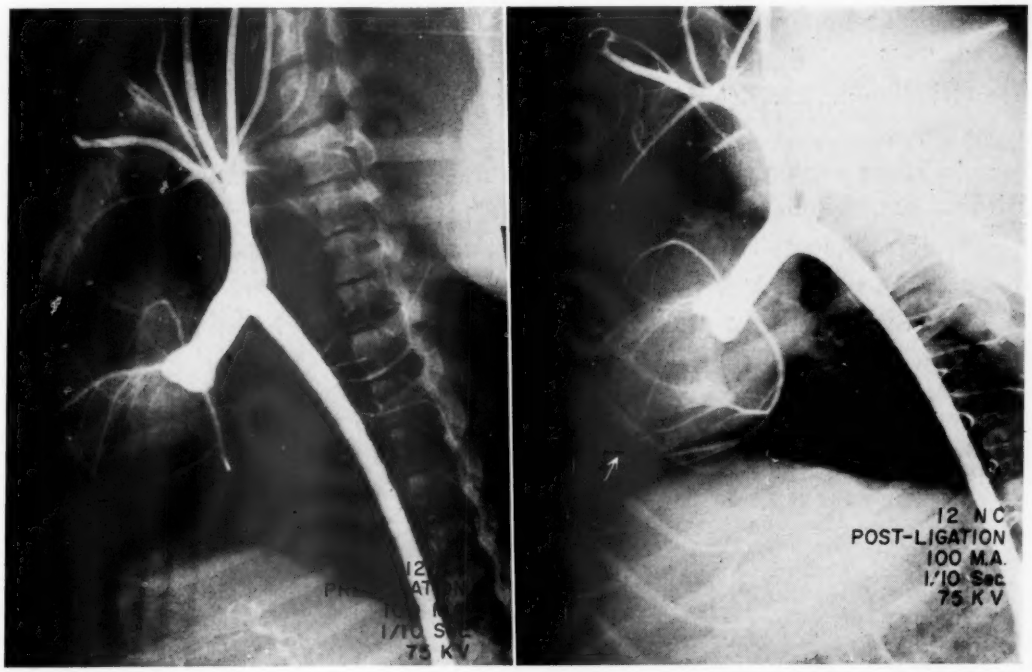

Fig. 9.—A comparison of preligation and postligation coronary angiograms in a dog 4 weeks following ligation of the left anterior descending coronary artery. A collateral channel between the anterior and posterior descending arteries is visualized (arrow) filling the entire left anterior descending artery retrograde.

The techniques of coronary angiography described not only permitted the detection of lesions created artificially (Fig. 8), but also aided in visualizing the development of collateral arteries to ischemic areas (Fig. 9).

These safe yet effective techniques of coronary visualization should permit the use of coronary angiography in the human patient with minimum risk. It is hoped that by the widespread use of coronary angiography in patients with coronary arterial insufficiency, a true picture of the pathologic anatomy will be derived. This information may then be used to select, modify, or develop surgical procedures to alleviate coronary arterial insufficiency. The selection of candidates for direct coronary arterial surgery versus the use of indirect methods of increasing myocardial blood flow would be based upon such angiographic studies as advocated by Thal[15] and recently carried out by Longmire.[9] This approach seems to be more logical than to recommend the same empirical procedure to all patients on the basis of "protective effect" of such procedures on acute coronary arterial ligation in dogs.

SUMMARY AND CONCLUSIONS

1. Various methods of coronary angiography were evaluated in a colony of 46 dogs.

2. The injection of 30 c.c. of 50 per cent Hypaque with an automatic injector through an intra-arterial catheter with the tip located at the junction of the brachiocephalic artery and the ascending aorta produced adequate visualization of the coronary arterial tree consistently.

3. This technique was improved and simplified by the use of temporary acetylcholine arrest. No detrimental effects resulting from the use of this drug were noted.

4. There was no added hazard to the use of coronary angiography (with or without acetylcholine) in the dogs with myocardial infarcts.

5. Experimentally induced lesions were depicted clearly.

6. It is proposed that the selection of candidates for direct coronary artery surgery versus indirect methods of increasing myocardial blood flow be based upon such angiographic studies.

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DISCUSSION

DR. HERBERT E. SLOAN (ANN ARBOR, MICH.).—Dr. Anlyan and his associates have demonstrated so clearly the superb visualization of coronary arteries which can be achieved with acetylcholine arrest. This technique may well be applicable to humans, but there would certainly be some question about its safety in patients with coronary artery disease and decreased myocardial oxygenation. The method certainly deserves wider application and this is to be expected from the excellent results presented here today.

In somewhat similar studies at the University of Michigan, attempts have been made to learn in dogs the optimum type and necessary concentration, volume, and speed of injection of contrast agent for adequate coronary artery visualization. Our results have suggested that 0.25 c.c. of 70 per cent Hypaque per pound, delivered in 3 heartbeats through a sidehole catheter in the base of the aorta, has provided reproducible opacification with sufficient clarity for surgical evaluation and negligible alteration of cardiac function. While the contrast produced has not been as sharp as that with acetylcholine arrest, it was felt that satisfactory opacification has been achieved, perhaps with decreased risk.

Efforts have been made to improve visualization of the coronary arteries by controlling several aspects of the circulation. Cardiac output has been reduced by occluding the inferior vena cava with a balloon catheter, increasing the intrathoracic pressure, and occluding the descending aorta with a balloon catheter. These measures resulted in slight widening of the coronary arteries. Bradycardia with prostigmine improved visualization. However, the use of vasodilators such as amyl nitrite has resulted in as much as 50 per cent widening of the coronary arteries, although there was no alteration of pulse or blood pressure. The use of amyl nitrite has improved visualization of the coronary arteries considerably with the technique described.

DR. OSLER ABBOTT (ATLANTA, GA.).—I wish to describe briefly the work which is being carried on at Emory University relative to this problem. This investigation is being done by Drs. William Sewall, Wade Shuford, and H. S. Weens. As shown in the first slide, a rubber balloon on a double lumen cardiac catheter is placed through the carotid artery into the ascending aorta of the dog. Following inflation of the balloon, contrast media is injected and a quite satisfactory method for obtaining high contrast in the coronary arteries is demonstrated. The difficulty is the matter of keeping the bag in a specific position and the possible dangers of temporary occlusion of the ascending aorta.

Further techniques investigated included the use of a polyvinyl catheter with a 2 mm. lumen and a removable metal stylette. Following introduction into the ascending aorta, consistent filling of the coronaries, including the secondary branches, was obtained with a dye injection carried out over a period of 0.5 to 2.0 seconds. However, the detail was inadequate to demonstrate collateral circulation or to give reliable information relative to localized coronary obstruction.

The next slide demonstrates the placement of the cardiac catheters with balloons attached near their tips and these catheters placed in the inferior and superior venae cavae

and inflated to obstruct the veins just prior to injection of the contrast media by means of another catheter in the ascending aorta. The resultant slowing of the linear velocity of blood flow in the aorta improved visualization of the coronary arteries. This method appears deserving of further study.

Our over-all experience suggests that the use of acetylcholine arrest appears to be the most promising technique. By this method good filling of the coronaries is obtained. We feel it is best to avoid placing the catheter too near the aortic valve and a distance of 2 cm. distal to the valve seems the optimal location.

If cardiac arrest is not utilized, injection time should include 2 to 3 cardiac cycles, and this has been satisfactorily accomplished by hand-operated lever system. In regard to the contrast media used, we prefer Hypaque.

We have carried out occlusions of the anterior descending coronary artery performing angiographic studies of the coronary bed before and after such occlusion. Our present techniques have frequently satisfactorily demonstrated localized area of occlusion, intercoronary collateral formation, and retrograde filling of the distal portion of the occluded coronary artery.

In conclusion we feel that significant progress is being made relative to coronary angiography.

DR. JACK A. CANNON (Los Angeles, Calif.).—Dr. Anlyan is to be highly congratulated for obtaining such very clear and thoroughly diagnostic coronary angiograms. Our experience with coronary angiography has not been this encouraging. Although, by our technique we were able to obtain accurate diagnostic angiograms, we found that the procedure itself imposed an unacceptable mortality of about 35 per cent when performed on dogs which had previously survived ligation of a major coronary artery. Consequently, I would like to ask Dr. Anlyan what his mortality has been in this procedure. In addition to a technique which produces accurate and diagnostic films, we must also impose the requirement that there be essentially no mortality and minimal morbidity if such a procedure is to be of diagnostic value in the human patient.

DR. FRANK GERBODE (San Francisco, Calif.).—I wish to speak on one point relative to angiography: our studies and those made by Dr. Herbert Abrams of our Department of Roentgenology lead us to believe that higher concentration of the contrast media, regardless of the brand, has a higher morbidity. There is also the desire to confine the contrast media to the aortic arch so that it will not escape into the cerebral circulation, where again higher concentrations are apt to produce symptoms. There is, however, a very pressing need for development of this type of diagnostic evaluation, for undoubtedly it will help us to find techniques which may have a more likely prospect of solving the surgical treatment of occlusive coronary disease.

DR. ANLYAN (Closing).—In reply to Dr. Cannon's question, two of the dogs in our initial pilot studies succumbed. The first dog died as a result of the use of a flexible catheter with a balloon which floated up with delivery of the radiopaque material into the cerebral circulation. The second dog died after the catheter had been erroneously placed in the left ventricle with resultant ventricular fibrillation. There was no mortality rate in the current group of 46 dogs.

CEREBRAL ISCHEMIA OF CENTRAL ORIGIN: RELIEF BY SUPCLAVIAN-VERTEBRAL ARTERY THROMBOENDARTERECTOMY

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NASHVILLE, TENN.

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OCCLUSION of the extracranial arteries which supply the brain was well described by Hunt[13] in 1914 as a primary cause of cerebral ischemia. Previously studied cases were cited. The term "intermittent cerebral claudication" was apparently first used in this publication. Intensive investigation of this facet of cerebrovascular disease has been pursued, however, only in recent years.[5, 9, 10-15, 18, 19, 22-26, 32, 33, 35, 37]

The term "aortic arch syndrome" was first applied by Frovig and Loken[12] (1951) to various diseases causing segmental occlusion of the major branches of the arch of the aorta. A component part of this syndrome was described as early as 1875 by Broadbent.[4] The recognition of its clinical and pathologic features, referred to by Shimizu[28] as "pulseless disease," has crystallized essentially in parallel with the knowledge of the frequency of the extracranial origin of cerebrovascular symptoms.[1, 2, 4, 6-8, 12, 16, 17, 20, 21, 27, 28, 31, 34, 36]

The increasing awareness of the occurrence of major segmental arterial occlusion in the cranial one-half of the body along with the rapid development of diagnostic and corrective procedures has resulted in a more aggressive approach to these problems. Reports of cases treated surgically appear with increasing frequency.[6-8, 10, 15, 19, 23, 25, 27, 32, 36] The majority have been concerned with the relief of carotid artery occlusion. In a smaller number which have dealt with the aortic arch syndrome, the surgical procedures have been directed primarily either at the relief of cerebral symptoms by attempting to improve carotid artery flow[6, 27] or at the relief of symptoms related to the upper extremity by improving subclavian artery flow.[7]

The present report is concerned with a variant of the aortic arch syndrome produced by atherosclerotic occlusion of the origins of the left subclavian and vertebral arteries. In the case described here symptoms referable to arterial insufficiency of the left upper extremity were present. The symptoms of greatest concern to the patient, however, were those related to the associated cerebral ischemia. Relief of both was obtained by thromboendarterectomy of the left subclavian and left vertebral arteries. This is, insofar as we can determine, the only reported attempt to relieve cerebral ischemia by a surgical approach to an occluded vertebral (and subclavian) artery alone. Since the importance of the vertebral arteries in maintaining adequate cerebral blood flow may not be widely recognized except by neurologists and neurosurgeons, it seems desirable that this be called to the attention of those interested in vascular surgery.

Read at the Twelfth Annual Meeting of the Society for Vascular Surgery, San Francisco, June 22, 1958.

CASE REPORT

J. A. W., Vanderbilt University Hospital Number 269272, a 49-year-old white man, was first admitted to the hospital June 1, 1957, to June 12, 1957. His second admission was Sept. 2, 1957, to Oct. 17, 1957. (Previous and subsequent admissions are irrelevant to the present discussion except as mentioned.)

History.—Approximately one year prior to his first admission the patient had first noted the gradual onset of weakness of the left upper extremity. He subsequently experienced discomfort in that extremity with excessive use which was relieved by rest. Later, in succession, he observed the left arm to be consistently cooler than the right with an associated decrease in perspiration and, 2 months prior to his first admission, the continuous absence of a left radial pulse.

Four months prior to his first admission the patient stated that he fell from a chair while turning and rising to speak to a visitor. There was no associated loss of consciousness. In retrospect he described pre-existing dizziness and an unsteady gait which he could not associate with his occasional alcoholic sprees. The latter symptoms preceded this episode, as best as could be determined, by a time interval of 4 to 6 weeks. The staggering gait became increasingly noticeable to himself and his associates. He later fell in a parking lot while assuming an erect posture after stepping from his car. Mental and emotional disturbances were described by members of his family. These were characterized primarily by inattentiveness and "drowsiness" interspersed with periods of irritability. A constant headache lateralized to the right occipitoparietal region and extending into the upper cervical region, unsteady gait, dizziness, poorly described visual disturbances, and the resulting inability to carry on a successful business were the symptoms which finally caused him to seek medical attention. The latter group of symptoms were noted to be the source of progressive difficulty for 2 or 3 weeks prior to his first admission. A speech disturbance (difficulty in precise articulation) was thought to be on the basis of previous surgical procedures related to lithiasis involving both submaxillary and both sublingual glands.

Physical Findings.—The patient was a tall but heavily built middle-aged white man who appeared chronically ill. His gait was unsteady and his movements, in general, were "shaky." Repeated examinations of his eyes, including ophthalmologic consultation, failed to reveal evidence of ocular pathology. Visual fields were grossly normal. Ophthalmodynamometric determinations were not performed. The common carotid artery pulsations in the neck were strong bilaterally; also the internal carotid artery pulsations as palpated from within the pharynx. There was no facial asymmetry. A hypersensitive carotid sinus reflex could not be elicited. The subclavian, brachial, and radial artery pulsations were normal on the right but were totally absent on the left. There was conspicuous absence of perspiration in the left axilla, along with coolness of the entire left upper extremity. Noticeable atrophy of the musculature of the left arm and forearm with a weak grip were present. Blood pressure recordings averaged 140/80 for the right arm, 150/90 for the right leg, and 150/90 for the left leg. They averaged 80/60 for the left arm until shortly before surgical intervention when no pressure could be recorded by the cuff method. No positive findings were noted on neurologic examination by a consulting neurologist other than some questionable predominance of reflexes of the right lower extremity, the unsteady gait, and weakness of the left arm and hand.

Pertinent Laboratory Findings.—Serology was repeatedly negative. Cholesterol was 177 mg. per cent and fasting blood sugar, 100 mg. per cent. Urinalyses and NPN were repeatedly within normal limits. Electrocardiogram was repeatedly "within normal limits."

Course.—Shortly after admission an arteriographic study of the aortic arch was made (Fig. 1) using a catheter passed via a femoral artery to the ascending aorta and injecting 16 c.c. of 90 per cent Hypaque with the pressure syringe. This study demonstrated occlusion of the left subclavian artery at its origin and patency of the remaining branches of the arch and both internal carotid arteries. It was felt following study of this patient

during his first admission (June, 1957) that, since he represented only a fractional picture of the aortic arch syndrome, surgical intervention was not justified. Diffuse intracranial arterial occlusion was thought to be the major source of his cerebral symptoms. The difficulties related to the left arm were not considered sufficient to justify a major operation, especially in view of the cerebral disease.

Following discharge the patient continued to be unable to carry on his successful business ventures and his symptoms persisted. He was readmitted to the Vanderbilt University Hospital 3 months later, primarily on the basis of our becoming aware of the importance of the vertebral arteries in the cerebral circulation as outlined by Hutchinson and Yates.[14] Although intracranial occlusive processes which might contribute to the decrease in total cerebral arterial circulation could not be excluded, it was felt that the presentation of a full head of pressure through the left vertebral artery would probably be beneficial.

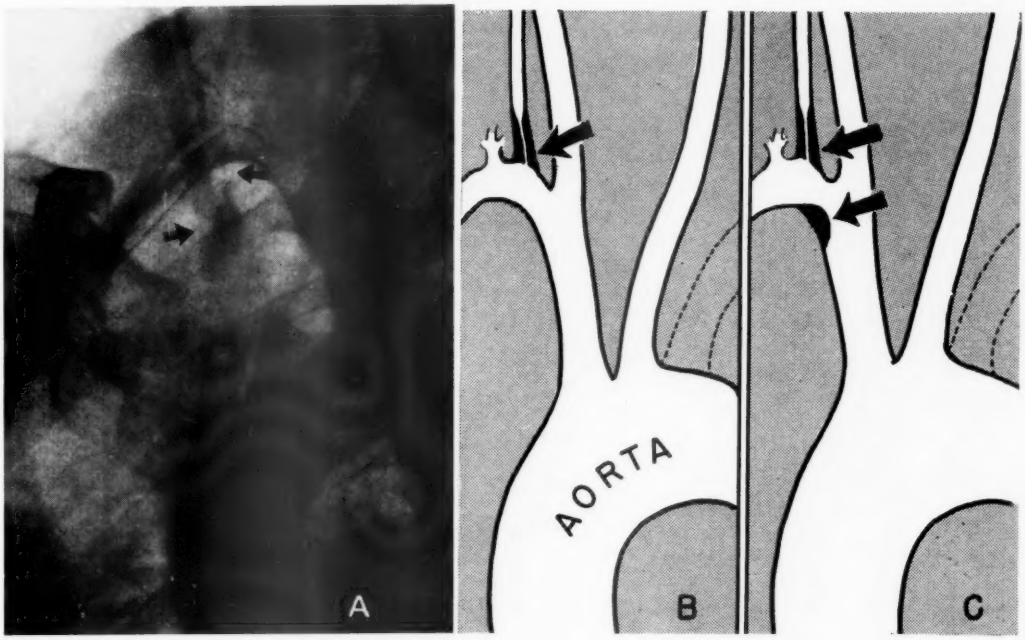

Fig. 1.—Retrograde aortography. *A*, Arrows point to narrowing of the origin of the right vertebral artery and a plaque, presence controversial, at the bifurcation of the innominate artery. The left subclavian (and vertebral) artery is not visualized. *B*, Narrowing of the origin of the right vertebral artery (arrow) illustrated diagrammatically. *C*, The more controversial plaque in the innominate artery (lower arrow) also diagrammed.

Operative Procedure.—Operation was carried out on Sept. 7, 1957, with the patient under endotracheal anesthesia. The patient was positioned in recumbency with his left side elevated slightly and the left arm extended. The incision (Fig. 2) extended upward in the neck along the anterior border of the right sternomastoid for approximately 3 inches, down the midline of the sternum to the third intercostal space, across the sternum at that level, with division of the left internal mammary vessels, into the third left intercostal space for approximately 6 inches, and along the left clavicle with subperiosteal resection of its medial one-half. The platysma muscle was divided vertically in line with the incision. The sternal origin and a portion of the clavicular origin of the left sternomastoid muscle were divided, along with the ribbon muscles on the left.

During the ensuing dissection, which exposed the left side of the aortic arch and the left subclavian and vertebral arteries, the vagus and phrenic nerves were isolated and retracted. Portions of the ansa subclavia were divided. The proximal left subclavian artery was completely occluded by a hard atheromatous plug at its origin from the aorta

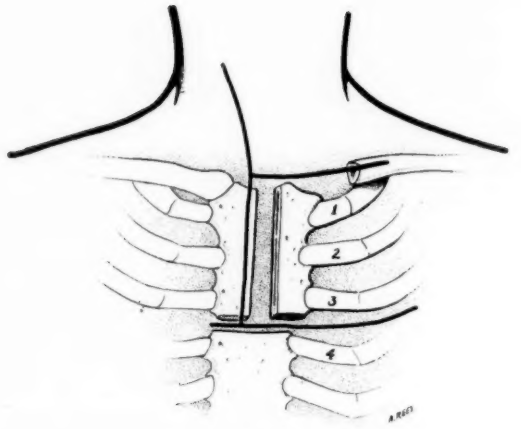

Fig. 2.

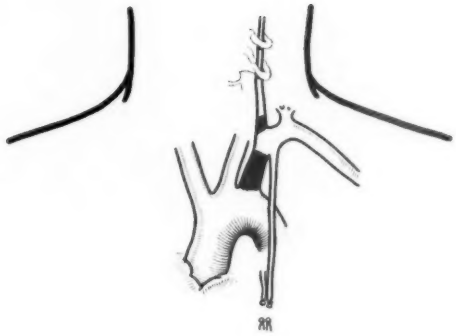

Fig. 3.

Fig. 2.—The incision used. Full description in text.
Fig. 3.—Operative findings. Occlusion of the left subclavian and the left vertebral arteries is illustrated.

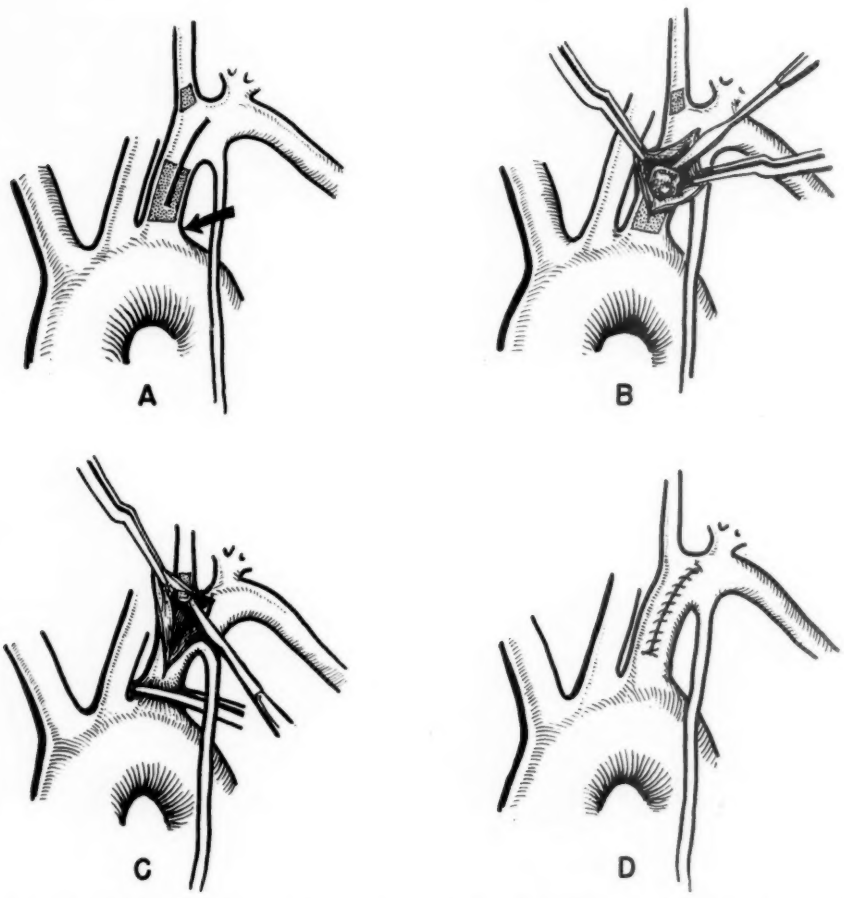

Fig. 4.—Thromboendarterectomy of the occluded left subclavian and vertebral arteries. The sequence is in error in that the left vertebral artery was cleared first. Description in text.

for a distance of approximately ¾ inch. The wall of the aorta surrounding the origin of the occlusive process was compressible. The subclavian artery distal to the occlusion was pliable and appeared normal. The origin of the left vertebral artery was occluded firmly, but for a distance of only ¼ inch or less. Distal to the occlusion the vertebral artery was a compressible vessel of normal appearance (Fig. 3).

Control of the vertebral and subclavian arteries distally was obtained with tapes and later with serrefine clamps. It was not technically feasible to occlude the origin of the left subclavian artery with a subtending segment of the lateral aortic wall because of the close proximity of the left common carotid artery. It was decided, therefore, to hold a Potts ductus clamp in position at the origin of the subclavian artery and to occlude it immediately upon removal of the occluding plug. An incision was made in the subclavian artery extending from the distal portion of the occlusion to a point opposite the origin of the vertebral artery (Fig. 4). A good backflow was obtained from the distal subclavian artery, but none from the vertebral. The atherosclerotic plug with adherent intima in the vertebral artery was first dissected free without difficulty. A brisk backflow was obtained then. The same procedure was repeated in removing the atheromatous obstruction from the origin of the subclavian artery. The Potts clamp was closed as the plug was removed after the first gush or two of blood from the aorta. It was necessary to tack the subclavian intima down with only 2 or 3 isolated mattress sutures of 5-0 arterial silk since the vessels distal to the sites of occlusion appeared to be entirely normal and the intima was adherent. Dilute heparin solution was injected into the distal arterial lumens. The arteriotomy incision was closed with a suture of 4-0 arterial silk. When the constricting devices were removed, an excellent pulsatile flow in the subclavian and vertebral arteries resulted without thrills.

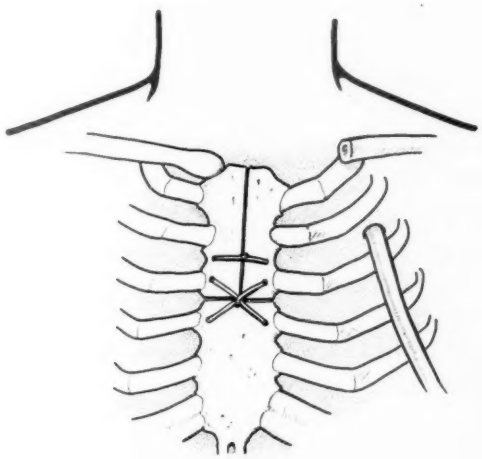

Fig. 5.—Stabilization of the sternum with three heavy wires of stainless steel threaded through drill holes. Drainage of the left pleural cavity.

The left pleural cavity was drained with a mushroom catheter. The sternum was stabilized with heavy wires inserted through drill holes as indicated in Fig. 5. The medial portion of the clavicle was discarded. The wound closure was routine.

Pathologic examination of the excised plugs of occluding material confirmed the clinical diagnosis of atherosclerosis with associated thrombus formation.

Postoperative Course.—Strong pulsations in the left radial artery were palpable in the immediate postoperative period. Recovery from the anesthetic was uneventful. A mild Horner's syndrome was noted and has persisted. When recovery had progressed sufficiently, the patient again began to read avidly, an activity which preoperatively had been extremely limited because of visual disturbances. Upon ambulation his gait was noted to be steady and has remained so. Headaches have not recurred and dizziness has

disappeared. The patient has returned to his normally vigorous business activities and has experienced no further difficulties with his memory. The emotional disturbances described preoperatively by his family and associates have ceased to be a problem. His dysarthria is markedly improved. This may have resulted from continued improvement after surgery for his multiple salivary gland disease. In the 9 months since operation the left arm has returned to normal in strength and size. Repeated examinations have revealed the blood pressure in the upper extremities to be equal and normal. The patient states at present (June, 1958) that he feels "better than I have in 10 years."

An annoying series of early postoperative complications were the development of an infection in the left clavicular region, which was drained, a succeeding mediastinitis resulting finally in an infection involving the horizontal component of the sternum-splitting incision and, as anticipated, malunion of that portion of the sternum. This series of difficulties resulted in a prolonged postoperative hospitalization. The wires used for stabilization of the sternum were subsequently removed. The horizontal limb of the sternal incision was restabilized after the infection was under control and solid union was achieved. There has been no disability resulting from the resection of the medial portion of the clavicle.

COMMENTS

The symptoms of arterial insufficiency in the left upper extremity of this patient were relatively mild. The same symptoms in relation to the aortic arch syndrome have been detailed by others and the general lack of severe ischemic manifestations commented upon.[6, 7, 12, 16, 17, 20, 21, 27, 28, 31, 36] The disability resulting from subclavian arterial occlusion, however, was the primary reason for surgery in the two cases recently reported by DeBakey and associates.[7] Vertigo has been described as the most common symptom of the aortic arch syndrome[27] and was a prominent feature of this case history. However, Shimizu[28] states that visual disturbances are the usual reason that such patients seek medical advice. Visual symptoms were distinct in this case but were not elicited with clarity. Their accentuation by exercise, so-called "ocular claudication," was not described by this patient. No ocular disease was noted such as the retinal arteriovenous anastomoses described by Takayasu[34] and Shimizu[28] or optic nerve atrophy.[20, 21] Facial atrophy was absent.

"Claudication of mastication,"[27] likewise, was not a feature of this case. "Orthostatic syncope" as listed by Davis[6] quoting from Martorell and Fabre[20, 21] was, on the other hand, a prominent feature. Headaches have been described as a frequent symptom of carotid occlusion[25] and the aortic arch syndrome.[6] They may be either intermittent (claudication?) or become continuous as with the patient under discussion. Mental or emotional disturbances may result from carotid artery disease alone,[25] may be associated with the aortic arch syndrome, may be symptomatic of "carotico-vertebral stenosis,"[14] or may be described as a consequence of vertebral or basilar artery stenosis alone.[30] Disorders of speech, associated predominantly with vertebral or basilar artery thrombosis,[30] could not be accurately evaluated in this patient because of the multiple surgical procedures related to salivary gland disease.

In regard to carotid artery pulsations, Rosegay[26] has stated that pharyngeal palpation "appears to be specific if the pulse is absent, but inconclusive for diagnosis if the pulse is present." Dunning[9] first described this physical finding. Others with considerable experience in the field of carotid artery surgery, such

as Rob and his associates,[25] have described this examination under any circumstances as "unreliable." The bilateral pharyngeal palpation of carotid artery pulsations in this case was partially responsible for the decision against surgical intervention on the first admission to the hospital.

The absence of radial artery pulsations, as observed in this patient on the left, has been repeatedly referred to in association with the aortic arch syndrome.[4, 20, 21, 27, 28] The inability to palpate a radial pulse has been previously noted to precede the inability to obtain a blood pressure by usual methods in the corresponding extremity.[27] The hypertension present in the lower extremities of other patients with the aortic arch syndrome[2, 20, 21] was probably absent in this case because of the relatively limited nature of the occlusive process.

A hypersensitive carotid sinus reflex[27, 28] could not be elicited. Weakness and atrophy of the upper extremity have been referred to,[7, 20, 21] but the relative absence of perspiration has not been emphasized. The lack of severe ischemic changes in the arm has already been commented on.

Syphilitic aortitis, with or without aneurysm, has been mentioned as a major etiologic factor in the aortic arch syndrome.[27] Its significance has decreased steadily as the treatment and prophylaxis of syphilis has progressed. A negative history and repeatedly negative serology essentially eliminated syphilis as an etiologic factor in this case.

The films obtained at the time of retrograde aortography, on the basis of subsequent review, have been variously interpreted (Fig. 1). The only unquestioned finding was the absence of dye in the left subclavian artery. What appears to be a narrowing of the origin of the right vertebral artery has been accepted by most who have reviewed the films (Fig. 1, *B*). The presence of a plaque in the innominate artery at the level of its bifurcation has proved less acceptable to our radiologic consultants (Fig. 1, *C*). However, either one or both of these findings must be valid, or else other occlusive processes not outlined probably exist since occlusion of one vertebral artery alone is almost certainly inadequate to account for the cerebral symptoms which this patient presented. The lack of visualization of the more cephalad portions of the carotid arteries leaves occlusive disease of these distal segments of the cerebral blood supply as possibilities. As mentioned previously, the pharyngeal palpation of internal carotid artery pulsations, as in this case, does not rule out carotid artery occlusion.

The incision used in this case is essentially that described by Shumacker.[29] As suggested by Elkin and Cooper[11] the resected medial portion of the clavicle was discarded. The finding of an occlusion at the origin of the vertebral artery, in addition to the subclavian, further strengthened our belief that the procedure would benefit the cerebral symptoms manifested by this patient. Further operative investigation of the central segments of the cerebral arterial supply was felt inadvisable because of the time consumed with the procedure described. The localized nature of the occlusive process made the choice of thromboendarterectomy an easy one. The decision against postoperative anticoagulant therapy might be questioned since the primary objective of the operation was the

re-establishment of normal flow through a relatively small artery, the left vertebral. Because of the high head of pressure at the sites of thromboendarterectomy, the excellent pulsatile flow, and the entirely normal appearance of the distal vessels, we felt anticoagulant therapy to be unnecessary.

The continued relief of cerebral symptoms in this case after combined subclavian-vertebral artery thromboendarterectomy seems to indicate the persistence of patency in both vessels. The vigorous radial pulse is evidence enough of patency of the subclavian artery. However, attention has been called to continued improvement in cerebrovascular symptoms after surgical attempts to relieve carotid occlusion despite the demonstration of thrombosis of the treated segments by arteriography or re-exploration.[15] Therefore, positive postoperative proof of patency of the left vertebral artery in this case is currently lacking since postoperative arteriography has not been done. The immediate and sustained relief of cerebral symptoms is difficult to ignore, however. Although they were not the primary impetus leading to surgery in this case, the symptoms related to the left upper extremity were disturbing to the patient. Their relief has been gratifying to him as it was to the patients described by DeBakey and associates.[7]

DISCUSSION

Confusion has resulted from the inclusion of diverse disease entities which cause occlusion of the major branches of the aortic arch under specific names such as "Takayasu's disease" and "Martorell's syndrome." The term "pulseless disease" was applied by Shimizu[28] to a group of cases falling into this general category but probably representing a specific disease entity involving, for the most part, young women. This condition was first described in part by a Japanese ophthalmologist, Takayasu.[34] Considerably later, Shimizu enlarged upon the description of this group of cases. At approximately the same time, Frovig and Loken[12] recognized the fact that a number of disease processes could result in the same symptom complex and first employed the term "aortic arch syndrome." Extensive reviews have appeared since.[17, 27]

Probably the clearest guide to the consideration of obliteration of branches of the aortic arch was provided by Ask-Upmark and Fajers.[2]

> The aortic arch syndrome is a denomination indicating the vascular conditions in cases when the aortic arch is involved so as to obliterate the big arteries arising from its convexity.
>
> This syndrome may be induced.
>
> 1. By Takayasu's syndrome ("young female arteritis").
> 2. By syphilitic aortitis.
> 3. By various other pathological conditions, such as severe arteriosclerosis.

Although a few changes in terminology would render this description more accurate, it does point with clarity to the multiplicity of etiologic origins of the same symptom complex. The case presented falls into the third category quoted, with the exception that the lesion was atherosclerotic rather than "arteriosclerotic" in nature.

Broadbent[4] in 1875 described the autopsy findings in a more advanced example of the aortic arch syndrome of atherosclerotic origin also occurring in a white man of middle age. His interest in the case was primarily that of explaining the bilateral absence of radial artery pulsations associated with good pulsations in the distal branches of the aorta. Cerebral symptoms were not referred to. A few quotations from his careful postmortem examination indicate features of the occlusive process which are being re-emphasized currently:

> "On further examination the innominate was found not only to be narrowed at its origin, but rigid. . . . Immediately above its origin the innominate enlarged to its usual size and possessed its normal elasticity." Referring to the left subclavian artery, . . . "here again atheroma had invaded the constricted orifice and rendered it rigid, while the artery beyond was healthy and of full diameter." Also mentioned is . . . "the occurrence of atheroma in an advanced stage at the narrowed orifices, while it was almost entirely absent elsewhere." Of interest relative to thrombendarterectomy is the observation that the "atheromatous patch" involving the innominate artery "separated readily from the outer tunic."

In 1914 Hunt[13] made the following interesting observations regarding the importance of proximal occlusion of the cerebral arterial blood supply in the production of cerebral symptoms:

> The object of the present study is to emphasize the importance of obstructive lesions of the main arteries of the neck in the causation of softening of the brain, and more especially to urge the routine examination of these vessels in all cases presenting cerebral symptoms of vascular origin. In other words, the writer would advocate the same attitude of mind toward this group of cases as toward the intermittent claudication, gangrene, and other vascular symptoms of the extremities and never omit a detailed examination of the main arterial stem.

The surgical approach to the relief of cerebral ischemia previously has been directed primarily at the carotid arteries, although mention of the contribution of the vertebral arteries has been made.[19, 36] Carotid artery occlusion was not demonstrated in the case presented. The attempt to relieve the cerebral symptoms manifested by this patient by the reestablishment of normal left vertebral artery flow was based primarily upon the evidence presented by Hutchinson and Yates[14] from autopsy studies in an article entitled "Carotico Vertebral Stenosis." In that article the following statement appeared: "Another important aspect of vertebral artery stenosis is that such stenosis alone may be responsible for infarction of the brain without either occlusion of the intracranial vessels or disease of the carotid arteries."

As found in this patient, atheromata were described as "particularly common at the origin of the vertebral artery from the subclavian artery."[14] The concept of a diminution in total cerebral blood flow in the production of cerebral symptoms was emphasized by these authors.

Biemond,[3] on the basis of arteriographic studies, has pointed out the fact that no fixed watershed exists between the blood supply of the carotid and vertebral arteries (Fig. 6). Although he notes further that the area of the posterior cerebral artery may be supplied by both routes, it is clear that the relief of carotid occlusion may not relieve symptoms secondary to vertebral

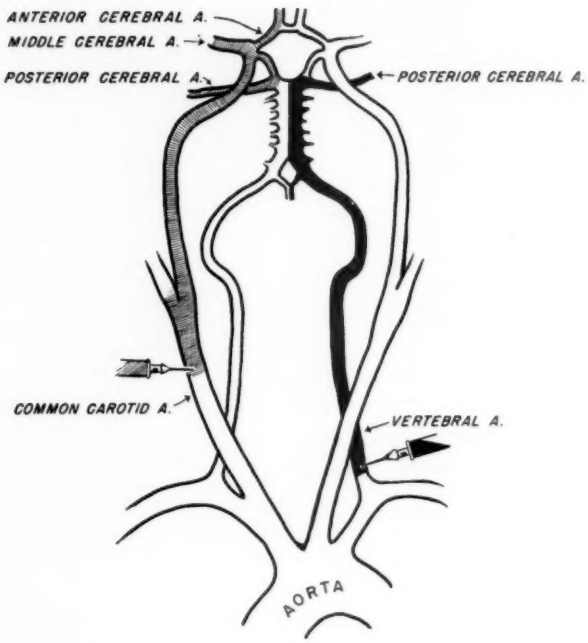

Fig. 6.—The lack of a fixed watershed between the vertebral and carotid artery flows demonstrated by vertebral and carotid arteriograms. Diagrammatic illustration.

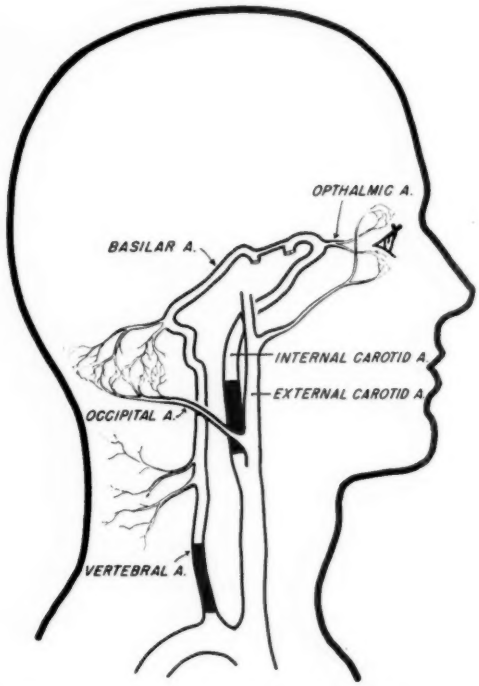

Fig. 7.—The collateral circulation to the brain with caroticovertebral stenosis. Diagram of collateral vessels demonstrated by vertebral and carotid arteriograms.

artery occlusion and that the reverse is also true. The available collateral circulation in cases of caroticovertebral stenosis, as again demonstrated by arteriographic studies, is between the external and internal carotid arteries via the ophthalmic artery[18, 22, 35] and between the vertebral and external carotid arteries via the occipital artery and the muscular branches of the vertebral artery[24] (Fig. 7). The studies of Hutchinson and Yates[14] would seem to indicate that the collateral channels from the external to the internal carotid artery are more effective than those in the vertebral artery.

The prompt relief of cerebral symptoms obtained by our patient by the reestablishment of left vertebral (and subclavian) artery patency alone further emphasizes the importance of the preoperative and operative evaluation of the status of the vertebral arteries in the surgical approach to cerebral ischemia. The aortograms obtained in this case (Fig. 1) probably did not outline accurately the total decrease in the central cerebral blood supply. It would seem, nevertheless, logical to perform such an examination in the majority of cases being evaluated for the surgical relief of cerebrovascular symptoms. A single injection of dye, properly administered, should outline occlusive processes involving the vertebral as well as the carotid arteries.

SUMMARY

A case of combined left subclavian and left vertebral artery occlusion of atherosclerotic origin occurring in a white man of middle age has been presented. Surgical intervention, consisting of thromboendarterectomy of the involved vessels, was directed primarily at the relief of the resulting cerebral symptoms. The success of the procedure further emphasizes earlier arteriographic and postmortem demonstrations of the lack of a fixed watershed between the vertebral and carotid artery flows.

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Discussion

DR. JESSE E. THOMPSON (Dallas, Texas).—I would like to comment on another extracranial cause of cerebral ischemia, namely, arteriosclerotic occlusion of the cervical portion of the carotid artery. These occlusions may be partial or complete and give rise to a variety of symptoms ranging from buzzing in the ear to frank hemiplegia with mental deterioration. I have had occasion to see 12 such patients recently in conjunction with our neurosurgeons. All have had arteriograms. Three patients have not been operated upon and 9 patients have had carotid endarterectomy carried out (slide). Five of these patients had good backflow from the internal carotid, three with partial and two with complete occlusions. Four have had excellent results and one a poor result. In two patients a temporary bypass polyethylene shunt was used to obviate cerebral damage. Four of the 9 patients had no backflow at the time of surgery and had complete occlusions. Functional

results have been variable in these patients. The problems here deal with the time interval from onset of the accident or symptoms to the restoration of carotid blood flow, the amount of irreversible brain damage present, and the presence or absence of a patent distal vasculature as evidenced by backflow from the internal carotid. An increasing awareness of this cause of strokes should bring patients in for study and treatment much earlier and will no doubt improve results.

DR. MICHAEL E. DE BAKEY (Houston, Texas).—I should like to express grateful appreciation to Dr. Scott and his associates for bringing to our attention the feasibility of restoring normal circulation in segmental occlusive lesions of the vertebral artery. The fact that cerebral arterial insufficiency, like that involving the lower extremities, may be due to well-localized atherosclerotic occlusive disease is now well established. Of particular significance is the fact, too, that such lesions may be located in the extracranial segments of the major arteries supplying the brain and are amenable therefore to effective surgical treatment. This is well demonstrated by the fact that, during the past 5 years in our experience with 43 cases in which this method of surgical treatment was employed, circulation was restored in all patients with the more proximal lesions occurring near the aortic arch and in all but one in whom the lesion was located at the origin of the internal carotid artery. There was one case in this series in which the occlusive process was located at the origin of the vertebral artery and was similar to that presented by Dr. Scott and his associates.

This patient was a 55-year-old white man who while fishing suddenly developed total blindness, paralysis of the right side, and partial paralysis of the left side of the body. These symptoms rapidly improved over the next few hours, and when he was admitted to the hospital, examination revealed incomplete homonymous hemianopsia of the right side. Arteriographic studies, as indicated by these slides, revealed complete occlusion of the vertebral artery on the right side and incomplete occlusion of the left limited to a small discrete segment of the vertebral artery at its origin from the subclavian artery. Operation was performed by one of my associates, Dr. E. Stanley Crawford, and consisted of endarterectomy performed through an arteriotomy opposite the origin of the vertebral artery as demonstrated by these drawings (slide). The patient's postoperative course was uneventful and improvement in his symptoms was immediately evident and continued until the time of his discharge from the hospital 10 days after operation. There was almost complete restoration of his visual defect and absence of all other symptoms. Arteriography following operation as demonstrated by this slide showed a normal lumen in the artery.

DR. SCOTT.—I would like to show two slides which emphasize further the important differences between the carotid and vertebral arterial contributions to cerebral perfusion. These differences are well understood, I believe, by our neurosurgical colleagues but may not be so well appreciated by those of us who are interested in vascular surgery. In the first slide which shows a normal carotid arteriogram you note the concentration of the opaque material in the arteries of the anterior portion of the brain with no opacification of vessels in the posterior portion. On the contrary, in the second slide which shows a normal vertebral arteriogram the reverse is seen with all the contrast material concentrated in the vessels of the posterior aspect of the brain and none in the anterior arteries.

DR. CATE (closing).—I would like to re-emphasize the importance of the preoperative and operative investigation of the vertebral arteries in dealing with this problem and the fact that retrograde aortography, having the virtue of a single injection, should be utilized most often in the preoperative investigation of cerebral ischemia.

LIMB SURVIVAL WITH AND WITHOUT DEFINITIVE SURGICAL TREATMENT IN OBLITERATIVE ARTERIAL DISEASE

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ARTERIAL insufficiency of the lower extremity, with very few exceptions, is due to arteriosclerosis obliterans. The diagnosis can be established by a history of intermittent claudication or of ischemic rest pain. The physical finding of absent peripheral pulses is of prime significance and, in the more advanced cases, rubor of the toes on pendency or localized areas of gangrene permit one to make the diagnosis at a glance.

The main problem is not one of diagnosis but of proper selection of therapy. Many patients with obliterative arterial disease of the lower extremity require no treatment whatever and others can be managed with the most conservative measures, such as instructions for better foot hygiene and the avoidance of harmful agents, such as externally applied heat. In the preservation of some limbs, lumbar sympathectomy seems to be the deciding factor. The restoration of the major arteries by a bypass graft or thromboendarterectomy may provide a most dramatic improvement both in the nutrition of the limb and in the ability of the patient to walk without pain. Unfortunately, however, attempts to clear an artery by thromboendarterectomy or to bypass an obstructed area with an arterial prosthesis are not always successful. Although these procedures may be carried out in such a manner as to minimize the risk of increasing the degree of ischemia, it has been our experience that the danger cannot be entirely eliminated. Finally, the fact that an arterial graft may function perfectly for several months, only to become occluded, is discouraging both to the patient and surgeon and emphasizes the need for better criteria for selecting patients for surgical treatment.

Having observed that the majority of patients with obliterative arterial disease require no specific therapy, our efforts have been centered on an attempt to determine which patients will benefit most by each of the therapeutic measures available. This led to the development of a method of grading the severity of the disease by clinical examination and then to an attempt to correlate the therapeutic results with the degree of ischemia existing at the time treatment was initiated.

This report analyzes the limb survival rate following conservative therapy, lumbar sympathectomy, and/or restoration of major arterial pathways by

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thromboendarterectomy or arterial graft. The method of estimating the severity of the disease by clinical examination alone has been previously reported[1] and is summarized as follows.

ESTIMATION OF DISEASE SEVERITY

Grade I. A Decrease in Amplitude of the Dorsalis Pedis and Posterior Tibial Pulse.—A diagnosis of obliterative arterial disease cannot be made by this finding alone unless there is a detectable difference on palpation between the amplitude of the pulse in the two extremities. A history of intermittent claudication, however, establishes the diagnosis and an appreciable diminution of the pulsations in these vessels is sufficient evidence for placing the limb in this grade.

Grade II. Absence of Both the Dorsalis Pedis and Posterior Tibial Pulse.—

Grade III. Absence of the Popliteal Pulse.—The popliteal is believed to be the most significant single pulse for evaluating a limb with arterial insufficiency[1, 5] and, when it is absent, the limb is considered to be in Grade III. Insofar as survival of the limb is concerned, no significant differences have been noted between the extremity with an absent popliteal pulse and the extremity with absence of the femoral or iliac pulse.

The criteria for assigning an extremity to the two next higher grades of arterial insufficiency are based upon the effects of ischemia on the tissues, and the presence or absence of peripheral pulsations is not considered. A limb without pulses may be perfectly viable, whereas ischemic necrosis may exist in a limb in which all named arteries are palpable. This apparent paradox may be explained by the fact that, although a palpable pulse is ordinarily a good qualitative index, it is not an absolute criterion of blood flow—that is, an artery pulsates immediately proximal to a point of occlusion despite the absence of forward blood flow; and on the other hand, large quantities of blood can flow through an artery distal to a block despite the absence of gross pulsation.

Grade IV. Rest Pain or Rubor of the Foot on Pendency.—Ischemic rest pain occurs in the toes or distal portion of the foot when it is in the horizontal position and it is relieved (initially, at least) when the foot is pendent. This phenomenon is believed to be due to the fact that the arterial inflow is so reduced in volume and pressure that it is unable to fill the capillaries in the presence of gravitational drainage through a normal venous outflow tract; and empty capillaries are truly ischemic. When the limb is in the pendent position, the capillaries remain filled due to gravitational force and the tissues are able to extract some nourishment from this residual blood.

Rubor may be difficult to detect when the red color is very faint; usually, however, its presence can be determined by a comparison of the two limbs.

Grade V. Continuous Pain, Petechial Hemorrhages of the Dorsum of the Foot, or Skin Necrosis.—When rest pain is advanced to the point that it is present continuously, the limb is considered to be in Grade V. Petechial hemorrhages of the dorsum of the foot or localized skin necrosis are also cardinal signs of the last stage of arterial insufficiency of the lower extremity. If the major portion of the limb is gangrenous, it is excluded from the grading system.

Diabetic Patients.—There can be no doubt that the presence of diabetes mellitus profoundly influences the course of obliterative arterial disease of the lower extremity. When estimating the severity of the ischemia on a clinical basis, we have considered the obliterative process to be of greater degree in the more distal portion of the limb in the diabetic patient. Support for this thesis is presented in Table IV, which shows that, in diabetic patients with ischemic rest pain, rubor, petechial hemorrhages, or skin necrosis, the popliteal pulse has been present in 56 per cent of the extremities. In nondiabetic patients, on the other hand, demonstrating a higher block as a rule, the popliteal pulse was present in only 15 per cent of the extremities in Grades IV and V. For this reason, extremities of diabetic patients with

absent dorsalis pedis and posterior tibial pulses have been considered to be in Grade III, whereas the same extremity in a nondiabetic patient would be Grade II. In Grades I, IV, and V, the criteria are the same for extremities of diabetic and nondiabetic patients. It has not been possible, however, to establish as unequivocal criteria for placing a limb of a diabetic patient in Grade II. If both the dorsalis pedis and posterior tibial pulse are present but diminished, the limb has been placed in Grade I. If the pulses are barely palpable or if one is absent and the other diminished, the limb has been considered to be in Grade II.

The factor of increased susceptibility to infection in diabetic patients is also of importance. In this regard, grading of the extremity is deferred until the infection has been controlled.

Because of these obvious differences and because there undoubtedly are other dissimilarities not yet clarified, the amputation rates of diabetic patients are analyzed separately.

Table I indicates the population studies and Table II the incidence in each grade of severity. There was no difference in incidence of each grade in the private patients or those seen in the vascular clinic of The Cincinnati General Hospital; therefore, the figures are combined. When the averages differ, they are considered separately, as in Table III. Of the 394 patients studied, 70 per cent were men and 23 per cent had diabetes mellitus. It is of interest that the sex ratio of the diabetic patients approached unity, 54 per cent were men.

TABLE I. TOTAL NUMBER OF PATIENTS WITH ARTERIOSCLEROSIS OBLITERANS AND THE NUMBER OF EXTREMITIES GRADED (1952-1957)

Number of patients:		
Private	230	
Clinic	164	
Total		394
Number of extremities graded:		
Private	387	
Clinic	292	
Total		679

TABLE II. THE INCIDENCE IN EACH GRADE IN 679 EXTREMITIES WITH ARTERIOSCLEROSIS OBLITERANS

GRADE	NUMBER OF EXTREMITIES	PER CENT
I	101	15
II	91	13
III	254	38
IV	133	19
V	100	15

TABLE III. THE SYMMETRY OF THE DISEASE BY GRADES IN 394 PATIENTS WITH ARTERIOSCLEROSIS OBLITERANS

	PRIVATE PATIENTS PER CENT	CLINIC PATIENTS PER CENT
Bilateral symmetrical	51	42
Unilateral disease (on clinical basis)	20	10
One amputation at first examination	7	14

TABLE IV. THE PRESENCE OF THE POPLITEAL PULSE IN GRADE IV AND V EXTREMITIES IN DIABETIC AND NONDIABETIC PATIENTS

	NUMBER EXTREMITIES	POPLITEAL PULSE	
		PRESENT	PER CENT
Diabetic patients	54	31	56
Nondiabetic patients	127	19	15

PROGRAM OF TREATMENT

Weight control and elimination of tobacco have been the recommendations for most patients with Grade I and II obliterative arterial disease. When a lumbar sympathectomy was performed, it was done as the second side of a bilateral operation in which the prime indication was more advanced disease in the opposite extremity. Lumbar sympathectomy was recommended, but rarely urged, for the patient with Grade III obliterative arterial disease, provided he was considered to be a good operative risk and under 70 years of age. During the latter half of the study, arteriograms were obtained on those patients with Graded III extremities who were being considered for surgical treatment. If the distal arterial tree offered an adequate "runoff," a grafting procedure or thromboendarterectomy (depending upon the size of the occluded segment) was recommended. If the "runoff" was poor, a lumbar sympathectomy was carried out.

Surgical therapy was recommended for all patients with Grade IV arteriosclerosis obliterans, unless there were strong medical contraindications. Advanced age in itself has become less and less a deterrent factor, as it has been recognized that a femoral-popliteal arterial graft can be inserted with almost negligible trauma and that even a lumbar sympathectomy (which requires a higher level of anesthesia) is certainly no more shocking to the patient than is a thigh amputation. Regardless of age, the presence of moisture on the foot or a rise in skin temperature of the toes following tibial nerve block is evidence that a lumbar sympathectomy will be of value.

Lumbar sympathectomy or restoration of major arterial continuity has been recommended and urged for all patients with Grade V extremities, unless it was believed that the operation might pose a serious threat to life, or when, because of poor general condition, it could be safely inferred that death would occur before the diseased limb would require amputation.

Conservative therapy in Grade IV and V extremities consists of recommendations for improved foot hygiene, use of a fungicide when necessary, nail and callus trimming, avoidance of tobacco in all forms, and strict and repeated warnings against external application of heat. In these advanced stages, swelling of the lower leg plays an important part in the deterioration of the limb. In the absence of cardiac decompensation, this swelling is almost always due to the fact that the patient sits in a chair day and night for relief of pain. Thus, the edema is predominantly gravitational. A vicious cycle of pain—pendent position for partial relief, swelling, increased pain, increased sitting, and so forth—is set up and unless it is broken it will make amputation necessary. In these instances a period of bed rest with sufficient analgesic medication to control pain may be helpful. Buerger-Allen exercises and therapeutic walking may be of benefit to some patients in this group because it keeps them active.

In Tables V through IX, the amputations of the conservatively treated patients are correlated with the grade of the disease present on initial examination. In the operative group, the amputations are correlated with the grade of the disease at the time of operation. All patients examined between August,

1952, and December, 1957, are included, except those seen only once. Also included are three major amputations on two patients that were performed in the first 5 months of 1958.

By limiting this analysis to the major amputation rate, it was possible to obtain follow-up data on almost all patients. Information as to whether the patient had come to amputation or had died was obtainable by telephone, mail, or search of the city death records.

RESULTS

Tables V and VI record the amputation rates for Grade I and II extremities to date. As noted above, lumbar sympathectomy was not considered necessary for the survival of the limb in the immediate future, but rather as the second side of a bilateral sympathectomy for more advanced disease of the opposite extremity. At least three of the 4 limbs lost in these two groups were the result of a sudden occlusion of the major arterial pathway. The low amputation rate in the conservatively treated extremities makes it difficult to demonstrate by statistical methods that any single specific therapy is of value in preservation of the limb. It would seem that conservative therapy is indicated, until a major arterial occlusion occurs, when immediate operative intervention offers an opportunity to save the limb.

TABLE V. THE MAJOR AMPUTATION RATE IN ARTERIOSCLEROSIS OBLITERANS IN GRADE I

	NUMBER OF EXTREMITIES	MAJOR AMPUTATIONS	PER CENT
Conservative therapy			
Nondiabetic	72	1	1.4
Diabetic	24	0	0
Lumbar sympathectomy			
Nondiabetic	3	0	0
Diabetic	2	0	0

TABLE VI. THE MAJOR AMPUTATION RATE IN ARTERIOSCLEROSIS OBLITERANS IN GRADE II

	NUMBER OF EXTREMITIES	MAJOR AMPUTATIONS	PER CENT
Conservative therapy			
Nondiabetic	71	2	2.8
Diabetic	8	0	0
Lumbar sympathectomy			
Nondiabetic	8	1	12.5
Diabetic	4	0	0

Table VII shows the amputation rate for Grade III extremities. At this point it must be emphasized that the group treated conservatively are not true controls for those treated surgically. There can be no doubt that recommendations for surgical treatment are more forcefully presented to those patients whose disease would appear to be progressive, nor can it be denied that the patient with more severe symptoms will be more amenable to a recommended operation. Furthermore, some patients were treated surgically only after their condition had deteriorated while on conservative therapy. But the fact that so

many patients have done well without surgical intervention points up the necessity for careful selection of patients for operative treatment.

TABLE VII. THE MAJOR AMPUTATION RATE IN ARTERIOSCLEROSIS OBLITERANS IN GRADE III

	NUMBER OF EXTREMITIES	MAJOR AMPUTATIONS	PER CENT
Conservative therapy			
Nondiabetic	151	5	3.3
Diabetic	45	3	6.7
Lumbar sympathectomy			
Nondiabetic	31	2	6.5
Diabetic	5	0	0
Graft or endarterectomy			
Nondiabetic	22	2	9.0
Diabetic	0	0	0

When ischemic rest pain or rubor is present, the amputation rate rises significantly (Table VIII). The fact that no limb of a diabetic patient in this group came to amputation following lumbar sympathectomy was an unexpected finding.

TABLE VIII. THE MAJOR AMPUTATION RATE IN ARTERIOSCLEROSIS OBLITERANS IN GRADE IV

	NUMBER OF EXTREMITIES	MAJOR AMPUTATIONS	PER CENT
Conservative therapy			
Nondiabetic	54	9	16.6
Diabetic	19	6	32.0
Lumbar sympathectomy			
Nondiabetic	23	5	22.0
Diabetic	8	0	0.0
Graft or endarterectomy			
Nondiabetic	18	4	22.0
Diabetic	1	1	100.0

The amputation rate in Grade V extremities is shown in Table IX. Here again, an element of statistical bias in favor of the conservatively treated patients must be pointed out. Had they lived a few months longer, some of the patients with Grade V extremities inevitably would have lost their limbs. On

TABLE IX. THE MAJOR AMPUTATION RATE IN ARTERIOSCLEROSIS OBLITERANS IN GRADE V

	NUMBER OF EXTREMITIES	MAJOR AMPUTATIONS	PER CENT
Conservative therapy			
Nondiabetic	43	27	63.0
Diabetic	27	13	48.0
Lumbar sympathectomy			
Nondiabetic	16	11	69.0
Diabetic	7	4	58.0
Graft or endarterectomy			
Nondiabetic	10	6	60.0
Diabetic	0	0	0.0

the other hand, surgical treatment was proposed only to those patients who were expected to live, so that their limbs were exposed to the danger of progressive disease for a longer period of time.

Despite the fact that our amputation rate following a grafting procedure or thromboendarterectomy is not significantly lower than is the rate following conservative treatment or lumbar sympathectomy, it should be noted that, when it is possible to restore major arterial continuity, the improvement is so marked as to remove all doubts that, when feasible, this procedure is the treatment of choice.

DISCUSSION

It is recognized that the amputation rate is a most inflexible criterion for estimating therapeutic results; however, it possesses the virtue of being objective. Certainly, it represents the end stage of the disease of the extremity just as mortality rates reflect the inexorable result of systemic disease. Less final criteria suggest a much more favorable effect of surgical treatment than is demonstrated in this study. Following lumbar sympathectomy, a significant rise in skin temperature of the foot and increase in the amplitude of digital pulsations as measured by a plethysmograph can be expected in extremities in Grades I, II, and III. In addition, the patient will almost invariably report marked improvement following the operation. Rest pain will frequently be relieved and rubor gradually subside in Grade IV limbs following sympathetic ganglionectomy. Some patients with Grade V extremities experience improvement after the operation. Intermittent claudication is influenced by many factors and it is difficult to obtain objective evidence of its amelioration following lumbar sympathectomy, but the complete disappearance of pain on walking following restoration of continuity of the major arterial pathway is unmistakable. Furthermore, its importance to the patient whose work requires him to walk a good deal cannot be minimized. The introduction of improved synthetic prostheses,[2-4] more discriminating selection of patients, and refinements of techniques all give promise of greater success in reducing disability and in preserving some limbs.

This study provides an abundance of evidence that the most important determinant of the result of treatment for extremities with obliterative arterial disease is the severity of the ischemic process when the patient first consults the physician. And since a very wide span exists between the limb with minimal disease and the one with impending gangrene, it behooves those interested in vascular problems to come to some agreement upon a description or definition of the various stages of obliterative arterial disease which are being treated. For example, a Grade III extremity in a nondiabetic patient is the limb most likely to have a localized segment of occlusion that can be removed or bypassed successfully. However, since only 5 of 151 extremities (3.3 per cent) in Grade III in this series have come to amputation when treated conservatively, it will be difficult to prove that any surgical procedure is responsible for the preservation of a limb in this group.

In the presence of ischemic rest pain or rubor (Grade IV) of the foot, however, the amputation rate rises sharply. And when the pain becomes continuous, and petechial hemorrhages or skin necrosis occur (Grade V), the amputation rate is in a totally different order of magnitude than for Grade I, II, or III extremities. Therefore it seems inescapably clear that, in order for the results of therapy, be it medical or surgical, to have any significance, the stage of the disease at the onset of treatment must be delineated. To meet this basic requisite, the clinical grading system employed in this analysis was devised.

SUMMARY

Arterial insufficiency of the lower extremity with very few exceptions is due to arteriosclerosis obliterans. It may vary so widely in severity that proper selection of therapy becomes the major problem, while the diagnosis is easily established by the history and physical examination. In an attempt to help solve the problem, 5 clinical stages of the severity of the disease have been delineated, and the number of amputations following conservative treatment, lumbar sympathectomy, and arterial grafting or thromboendarterectomy has been correlated with the stage of the disease existing at the time therapy was instituted.

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DISCUSSION

DR. NORMAN E. FREEMAN (San Francisco, Calif.).—Dr. Cranley and his associates have performed a real service in establishing a clinical method of grading the severity of the obliterative arterial disease in patients with arteriosclerosis obliterans. Our findings are entirely in agreement with theirs as far as Grades I, II, and III are concerned.

In their higher grades we have been impressed in the last 7 years with the usefulness of the reactive hyperemia test. By means of this test the filling pressure in the smaller vessels of the extremity can be quantitatively measured as the level above the heart to which the feet must be lowered before flushing will take place, following a temporary period of circulatory arrest. It has been our observation that, in patients with rest pain or open lesions independent of the presence or absence of the peripheral pulses, healing will take place if the filling is present when the extremities are above 35 cm. above heart level. If, however, filling does not take place until the feet are lowered below the 35 cm. level, conservative amputations are useless and major amputation has resulted. On the other hand, in the absence of rest pain or an open lesion, it is remarkable how long patients can get along with their ischemic extremities without coming to major amputation.

DR. BERT SELIGMAN (Toledo, Ohio).—Diabetic neuropathy in young people may be complicated by gangrene of one or more toes, the dorsum of the foot, or the heel, and with it full bounding pulses may also be present, even the dorsalis pedis and posterior tibial. With this picture in mind, how do you distinguish between arteriosclerosis obliterans complicated by diabetes and the patient who does not have arteriosclerosis obliterans but does have diabetic neuropathy?

DR. ORMAND C. JULIAN (Chicago, Ill.).—It could be suggested that some deficiency may exist in control of the group with definitive surgical treatment due to selection of patients for surgery as well as to the kind of surgical treatment given. This latter consideration basically depends upon whether the techniques of 1951 or of 1958 were used. All groups working in this field are aware of the improvement in results due to improvement in technique.

The experiences which are reported by our group and by most others are contrary to the suggestion of the authors that reparative surgery should be reserved for advanced stages of peripheral arteriosclerosis. We hold that patients whose disability is limited to intermittent claudication are those in whom the most reliable and lasting benefit is obtained.

DR. CRANLEY (closing).—We have recognized the value of Dr. Freeman's reactive hyperemia tests, but in this study we have tried to limit all testing to that which can be observed by history and physical examination.

In regard to Dr. Selegman's question, in our experience, the diabetic neuropathy more or less represents various degrees of anesthesia, and we have not attributed severe rest pain to neuropathy. In our opinion, rest pain is due to ischemia, and it is believed to be due to the fact that the arterial inflow is so reduced in volume and pressure that it is unable to fill the capillaries in the presence of gravitational drainage through a normal venous outflow tract. This pain is relieved when the foot is pendant, because the capillaries remain filled, due to gravitational force, and the tissues are able to extract some nourishment from this residual blood.

In regard to Dr. Julian's comments, there is really little difference of opinion. If a patient is incapacitated by intermittent claudication, then, by all means, direct arterial surgery is indicated. However, intermittent claudication does not incapacitate all patients. Many have it for years without evidence of progression and are able to carry out their normal activities. It is not clear that surgical therapy is desirable for all such patients unless, of course, survival of the limb is threatened by progression of the disease.

THE RATE OF HEALING OF ARTERIAL AUTOGRAFTS

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THE rate of healing of a wound and the effect of local and systemic factors that influence healing can be measured by several methods. In sutured wounds, the rate of healing may be computed by determining the rate of gain in tensile strength, and in open wounds by measuring the changing surface area by planimetry.[2] These methods probably measure the increasing content of collagen as wound healing progresses; for it has been shown that the hydroxyproline content of wounds, an amino acid almost exclusively found in collagen, roughly parallels the rate in gain of tensile strength.[4] Because physical and biochemical changes correlate well in the healing wound, either may be measured to quantify the rate of healing. The factors which will determine the method of choice are the type of wound, whether superficial or deep, closed or open, and the anatomy of the tissue, whether tubular or solid.

Since the turn of the century and especially during the last decade, with the renewed interest in reconstructive vascular surgery, there has been a considerable accumulation of knowledge concerning the healing of sutured blood vessels, the fate of various grafts and prostheses, and the technical features of operative procedures. In spite of extensive research in this field of surgery, there is little quantitative information concerning the rate of healing of sutured blood vessels. Lowenberg and Shumacker (1949)[8] measured the rate of healing of arteries repaired by end-to-end anastomosis in dogs and found a curve of healing approximating that of other tissues.

The subject matter of this paper is the rate of healing of arterial host-autograft anastomoses in dogs. Fresh autografts appear to survive intact and they are capable of increasing their diameter in the growing animal.[8, 11] The same healing process that occurs in a lateral arterial wound takes place at the proximal and distal anastomoses of an autograft.[3] Beyond the suture lines the microscopic appearances of the arterial autograft are indistinguishable from the adjacent normal vessel.[1] Since several observers have noted that a healed autograft resembles a normal artery in nearly all respects it would seem reasonable

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to expect that a curve of the rate of healing of a host-autograft anastomosis would approximate that of a divided artery repaired by end-to-end suture. The results of this study, however, revealed some significant differences.

In this experiment the rate of healing was determined by measuring the gain of tensile strength. This principle has been applied to determine the rate of healing of wounds of skin, fascia, tendon, muscle, and bowel.[7, 10]

CONSIDERATIONS IN DETERMINING THE TENSILE STRENGTH OF ARTERIAL ANASTOMOSES

The strength of an arterial anastomosis may be measured by one of two methods. In one, the anastomosis is distended with air or water and the bursting pressure recorded. Although not requiring any elaborate apparatus, this method has certain disadvantages. The entire anastomosis is used in one test, and only one determination can be made on each specimen. If histologic sections are to be studied, the microscopic appearances may be distorted by the stresses imposed on the vessel during testing. A further disadvantage of the bursting method is that the point of rupture cannot always be recorded with certainty because leakage may occur without rupture. Within the first few days of healing, the integrity of an arterial anastomosis is dependent upon several factors. The strength, quantity, and type of suture employed, the suture holding power of the artery, and the presence of blood clot at the suture line all contribute to make the anastomoses "watertight." Blood clot has little strength and is easily dislodged, and, consequently when the anastomosis is distended, leakage may occur without actual disruption of the suture line. The recorded pressure will thus represent the strength of a part of the anastomosis and not the whole.

Another method of testing the strength of an anastomosis is to measure the force required to pull the anastomosis apart. The anastomosis, or a segment of it, is placed in a tensiometer and subjected to a load in a linear direction. In the present study excised portions of the anastomosis were tested. This allowed both multiple tensile strength determinations and histologic examination on a single specimen.

Tensile Testing.—For dependable results, a tensiometer should conform to certain specifications. The ideal tensiometer is one capable of controlled extension rates and has an instantaneous recording system. The results obtained with manually operated tensiometers, whose rate of extension cannot be accurately controlled, may not be consistent because the rate of extension influences the breaking strength of a tissue. The tensile strength of a tissue is also influenced by its water content and temperature. Consequently the tissue should be kept wet during testing and the determinations carried out in an environment in which the temperature and humidity are controlled.

The method of securing the specimen in the jaws of the tensiometer is also of importance. If the jaws are too tight the specimen often breaks at the jaws of the tensiometer on extension ("jaw break") resulting in a false breaking value. On the other hand, if the specimen is not securely fixed in the jaws, it will slip on extension ("jaw slip") and a false elongation value will be recorded.

Controls.—The rate of gain in strength of a sutured artery is best determined by expressing the tensile strength of the anastomosis as a percentage of the normal (control) artery. Wide variations of tensile strength may be encountered not only in different arteries in the same animal but also in different regions in the same artery,[5] and it must not be assumed that even the same artery can act as the control. The tensile strength (force per unit area) of the abdominal aorta, for example, is greater than that of the thoracic aorta because of the relatively greater collagen content in the former. The thoracic aorta has a higher proportion of elastic tissue whose tensile strength is less than that of collagen. In this study the common carotid artery of the dog was selected as the artery of choice. The diameter, thickness, and composition of this artery are fairly uniform throughout in the same animal and thus its tensile strength does not vary widely in different parts of the artery.

In an experiment of this nature the carotid artery had further advantages. Both vessels could be exposed through a single skin incision and skin wounds of the neck heal well. Because the common carotid artery has no significant branches, potentially weak areas of the arterial wall are eliminated. Should thrombosis of one or even both carotids occur, the dog survives without any apparent impairment of health. Being a small diameter vessel (3 to 4.5 mm.), it is a critical testing area for operative technique.

MATERIALS AND METHODS

The experiments were carried out on adult mongrel dogs. Their weights varied from 25 to 35 pounds and they were fed on a standard laboratory diet. The animals were anesthetized with veterinary Nembutal (0.6 Gm. per kilogram) administered intravenously. Most of the dogs received an intramuscular injection of 600,000 units of penicillin and 1 Gm. of streptomycin at the time of operation.

After careful shaving and preparation of the skin, a midline incision 3 inches in length was made in the lower half of the neck. Skin towels were applied to the wound edges and the instruments used up to this stage were discarded. After division of the general investing layer of deep cervical fascia, the carotid sheath on one side was exposed in the plane between the sternomastoid and pretracheal muscles. A 2-inch segment of artery was mobilized by stripping the loose periadventitial tissue. Small bulldog clamps were applied to the artery and a 1¼-inch segment of vessel was excised between the clamps. The lumen of the autograft was irrigated with isotonic saline and was sutured back into position using an end-to-end anastomosis employing 6-0 interrupted braided silk sutures. Sixteen sutures were used for each anastomosis. On releasing the arterial clamps, bleeding from the anastomoses was occasionally brisk in spite of the closely applied sutures, but this was easily controlled by applying light digital pressure over a gauze sponge. The same procedure was then carried out on the opposite carotid artery. Anticoagulants were not used and antibiotics were not administered postoperatively. Carotid arteriography was carried out in some dogs using a catheter inserted via the right brachial artery and the tip guided into the aortic arch opposite the origin of the brachiocephalic trunk.

After varying periods of time each animal was reanesthetized, and both autografts and adjacent normal artery were dissected carefully and the presence or absence of pulsation noted. Each specimen was removed en bloc, incised longitudinally, and examined for evidence of thrombosis, rupture, stenosis, or dilatation. A segment of anastomosis was excised for histologic examination and the rest of the specimens were sealed in polythene bags and stored at −70° F. until ready for tensile strength studies. Testing of the arteries could not be carried out immediately following their removal because the tensiometer used in this study

was located at some distance from the laboratory and was not available at all times. The possible effect of deep freezing and delay in testing on the tensile strength of the arteries will be discussed later.

DETERMINATION OF TENSILE STRENGTH

The tensile strength determinations were performed with the use of an Instron tensiometer, a highly sensitive electronic weighing system employing strain gauges for detecting and recording the tensile load applied to the material under test. The sample to be tested is secured in the upper and lower jaws of the tensiometer. The upper jaws are stationary and the lower jaws move at a prefixed velocity. An instantaneous load-elongation curve is recorded.

The arteries were removed from the polythene bags and thawed by immersion in water for at least 15 minutes before testing. The temperature of the room was 70° to 72° F. and the relative humidity 55 (±5) per cent. The loose areolar tissue surrounding the graft and adjacent normal artery was carefully removed by sharp dissection. In the region of the anastomoses, the black silk sutures indicated the external surface of the artery, and the depth of dissection was limited to this plane.

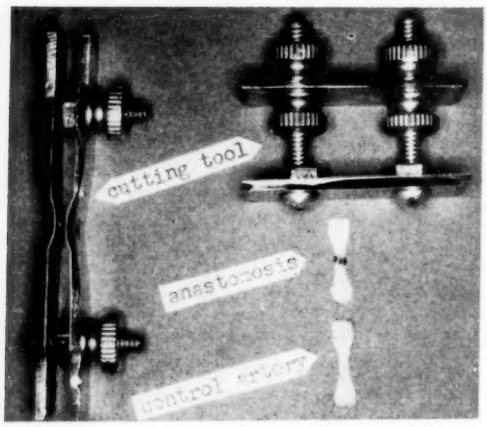


Fig. 1.

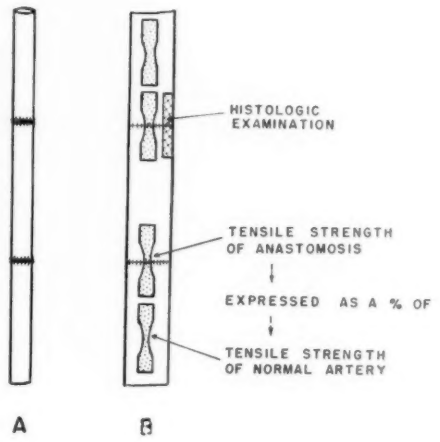


Fig. 2.

Fig. 1.—The instruments used for punching out dumbbell-shaped segments from each anastomosis and control artery. The position of the blades can be varied if necessary.

Fig. 2.—*A* is a diagram of the intact autograft and adjacent host vessel. In *B* the artery has been incised longitudinally and laid flat to form a ribbon. The stippled areas are segments of artery which were removed and tested for tensile strength. The tensile strength of each anastomosis was expressed as a percentage of the adjacent normal artery (control). The cross-hatched area represents a segment of anastomosis that was removed for histologic examination.

Using a specially designed instrument (Fig. 1), dumbbell-shaped segments were punched out of each specimen, so that the anastomosis lay across the narrow waist of the segment (Fig. 2). Arterial segments of this configuration were used to avoid jaw slip and jaw break and to concentrate the applied stress in the region under test. The cross-sectional area of each specimen was determined at the segment's waist. The width of the punch was kept constant ($\frac{5}{64}$ inch) but could be varied if necessary by adjusting the position of the blades.

The thickness of each anastomosis and normal artery was measured by placing the segment between two narrow pieces of file card of known thickness, and the total thickness was measured with a micrometer accurate to 0.001 inch. The use of the semirigid card allowed the observer to determine the end point more accurately and to avoid undue compression of the specimen. Although the width of the punch was constant, the width of the specimen was always checked and measured to the nearest $\frac{1}{128}$ inch. The measurements were always made by one observer.

Each specimen was then secured in the jaws of the tensiometer with a strip of medium grade emory cloth interposed between the jaws and the artery; the abrasive surface was in contact with the artery. This increased the frictional resistance between the artery and the jaws and thereby reduced jaw slippage to a minimum. At the same time, it was no longer necessary to tighten the jaws excessively and consequently jaw breakage was virtually eliminated. The specimens were kept wet throughout the testing. The following settings of the Instron were used: (a) a constant gauge length ($\frac{3}{16}$ inch), which is the initial distance between the two jaws and corresponds to the unstretched length of the artery under test, (b) a lower jaw speed of 2 inches per minute, (c) a chart speed of 10 inches per minute, and (d), a range of sensitivity from 0 to 2,000 Gm. The specimens of artery were subjected to a linear force until rupture occurred, and a simultaneous load-elongation curve was obtained for each test.

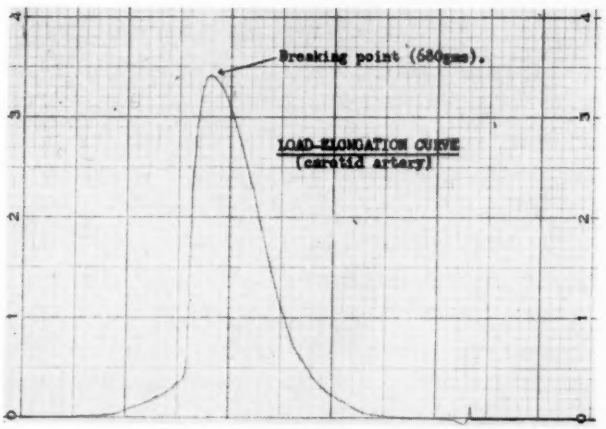


Fig. 3.—A typical load-elongation curve of a segment of carotid artery. The graph paper moves from right to left.

Examination of the load-elongation curves (Fig. 3) revealed the breaking load (grams) and breaking elongation (inches). Knowing the cross-sectional area and breaking load of each anastomosis and corresponding normal artery, the tensile strength of each was calculated and expressed in grams per square inch. The tensile strength of each anastomosis was expressed as a percentage of the corresponding normal artery (control). The mean tensile strength of the four anastomoses in each dog was then plotted against the age of the anastomoses and a curve was obtained for the rate in gain of strength.

RESULTS AND DISCUSSION

Twenty-four fresh arterial autografts, comprising 48 host-autograft anastomoses, were studied in 12 dogs. The duration of implantation varied from 0 to 56 days.

Gross Appearance of the Autografts.—Twenty-three of the 24 autografts were patent at the time of removal, a patency rate of 96 per cent. The occluded graft occurred in a dog which developed a wound infection and had been implanted for 3 days. At the proximal and distal anastomosis of the contralateral autograft there was a small mural thrombus. In none of the grafts was there any evidence of suture line disruption, stenosis, dilatation, or aneurysm formation. The intima of all was smooth and intact, and in fact there was nothing to distinguish the graft from the normal artery (Figs. 4-9). On the external surface of some of the older autografts, small vascular channels could be discerned which resembled the vasovasorum of the normal artery (Fig. 10). Fig. 11 is a bilateral carotid arteriogram of an 8-week dog. Both carotid arteries are of normal caliber.

Microscopic Appearance of the Autografts.—The healing process at the anastomoses resembled that of healing wounds in general. Shortly after suture, blood clot was deposited at the line of suture which after a few days showed evidence of organization (Fig. 12). With the passage of time the suture line was composed of fibroblasts and collagen fibers lined internally by endothelium (Fig. 13). In some cases, except where sutures were present, the junction was almost imperceptible and the transition from graft to normal artery was difficult to delineate (Fig. 14). Only with the use of elastic tissue stains could the junction be seen. Continuity of the elastic fibers across the anastomoses was seen in some of the older specimens. Beyond the suture lines the autograft was indistinguishable from the normal artery (Figs. 15 and 16). That the grafts had become vascularized was clear in some specimens from the presence of vasovasorum in the media containing red cells and foci of recent hemorrhage, the latter undoubtedly from trauma during excision. The elastic laminae and muscle fibers were well preserved, and the intima was intact. There was no evidence of calcification or degeneration, neither did we expect to find any, for the period of implantation was not long. In homografts, however, degenerative changes may occur within a few weeks.

The reaction of the tissue to the suture material was variable although the same suture material was used throughout. Around some sutures the reaction was chronic, as characterized by giant cells of the foreign body type, plasma cells, and reticulum cells. Occasionally the surrounding reaction was acute; numerous polymorphonuclear leukocytes and red cells surrounded the suture material. Occasionally no reaction was evident. When the reaction was marked, it would be difficult to incriminate the silk per se because the sutures were waxed.

The Rate of Gain in Strength of the Anastomoses.—Table I shows the data obtained for the tensile strength of each anastomosis and its corresponding control and the duration of implantation. The tensile strength of each anastomosis

TABLE I. THE TENSILE STRENGTH DATA OF THE ANASTOMOSES AND CORRESPONDING NORMAL ARTERIES CALCULATED IN GRAMS PER INCH^2

DOG NUMBER	AGE OF ANASTOMOSIS (DAYS)	TENSILE STRENGTH OF ANASTOMOSIS (GM./IN.^{2} × 10^4)	TENSILE STRENGTH OF NORMAL ARTERY (GM./IN.^{2} × 10^4)	TENSILE STRENGTH OF ANASTOMOSIS (PER CENT OF NORMAL)	MEAN TENSILE STRENGTH OF ANASTOMOSES (PER CENT OF NORMAL)
9	0	9.83	38.80	25.34	17.01
		10.17	69.68	14.60	
		5.13	38.80	13.22	
		5.00	38.80	12.89	
1	1	11.89	62.12	19.14	19.11
		6.84	48.57	14.08	
		10.26	35.90	28.58	
		4.68	31.94	14.65	
2	2	6.50	33.70	19.29	22.55
		13.13	75.00	17.47	
		11.67	37.50	31.12	
		11.00	49.25	22.34	
3	3	6.25	50.68	12.33	18.48
		6.77	28.64	23.64	
		6.00	35.38	16.96	
		9.71	46.30	20.97	
4	4	11.19	55.56	20.14	18.61
		8.20	46.43	17.66	
		11.20	62.14	18.02	
		15.50	jaw slip	—	
10	7	6.67	35.00	19.06	22.03
		8.94	35.00	25.54	
		9.21	34.33	26.83	
		6.84	41.00	16.68	
11	11	8.46	24.33	34.77	27.42
		6.60	27.88	23.67	
		10.38	35.00	29.66	
		10.63	49.29	21.57	
9	14	12.79	38.18	33.50	36.08
		16.49	38.18	43.19	
		10.15	27.92	36.35	
		12.63	40.38	31.28	
8	21	11.92	20.20	59.01	44.21
		9.26	27.00	34.30	
		8.46	29.47	28.71	
		10.00	18.24	54.82	
5	28	13.06	29.75	43.90	61.88
		18.79	25.50	73.69	
		17.96	26.25	68.42	
		15.38	25.00	61.52	
7	42	16.53	23.08	71.62	64.74
		26.19	48.15	54.39	
		28.33	27.32	58.84	
		20.25	46.60	74.12	
6	56	25.00	39.14	63.87	70.77
		15.50	21.62	71.69	
		21.43	41.97	51.06	
		19.13	19.83	96.47	

In Column 5 the tensile strength of each anastomosis is expressed as a per cent of the normal. The mean tensile strength of the four anastomoses in each dog is found in Column 6 in chronological order.

Fig. 4.

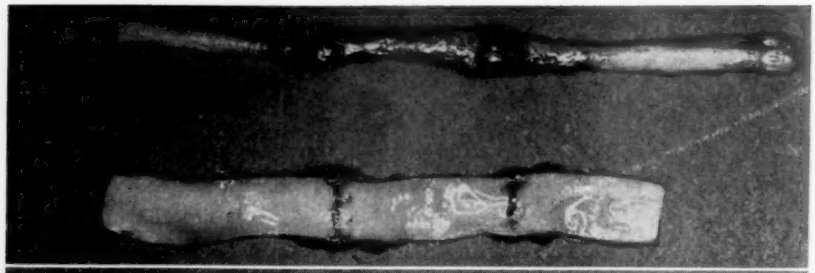


Fig. 5.

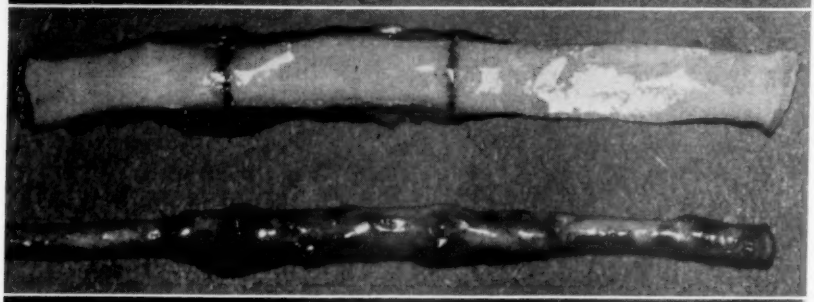


Fig. 6.

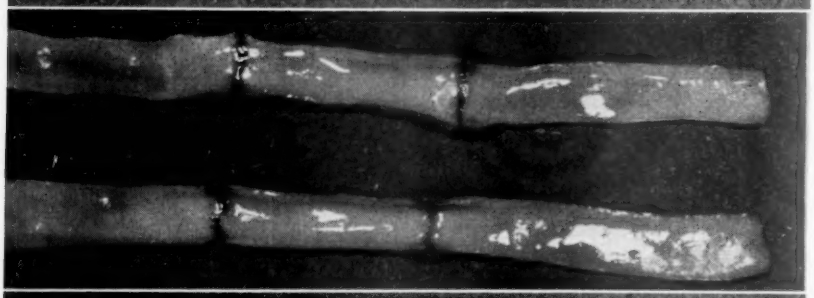


Fig. 7.

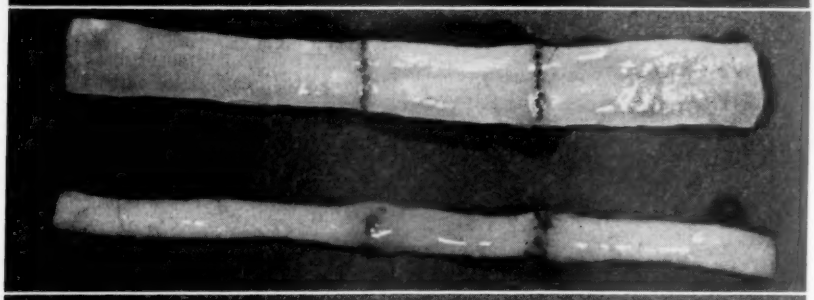


Fig. 8.

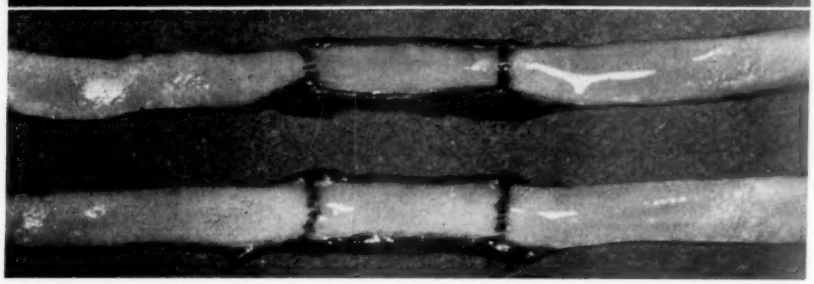


Fig. 4.—Bilateral carotid autografts (11 days). The lower autograft has been incised longitudinally to show the intimal surface.

Fig. 5.—Bilateral carotid autografts (2 weeks).

Fig. 6.—Bilateral carotid autografts (3 weeks).

Fig. 7.—Bilateral carotid autografts (4 weeks).

Fig. 8.—Bilateral carotid autografts (6 weeks).

Fig. 9.

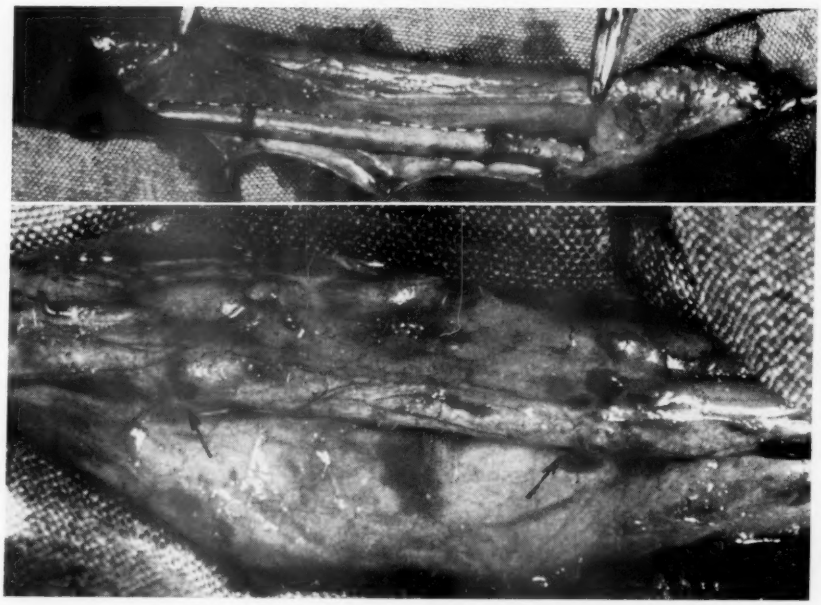


Fig. 10.

Fig. 9.—A carotid autograft in situ 4 days after operation.

Fig. 10.—An 8-week-old autograft in situ. Note the vascular channels on the external surface of the autograft which resemble the vasovasorum of the adjacent normal artery. The arrows indicate the anastomoses.

Fig. 11.—A bilateral carotid arteriogram. The arrows point to stainless steel sutures which were inserted at the time of operation to mark the levels of the proximal and distal anastomoses of the autografts. There is no evidence of stenosis or dilatation.

Fig. 12.

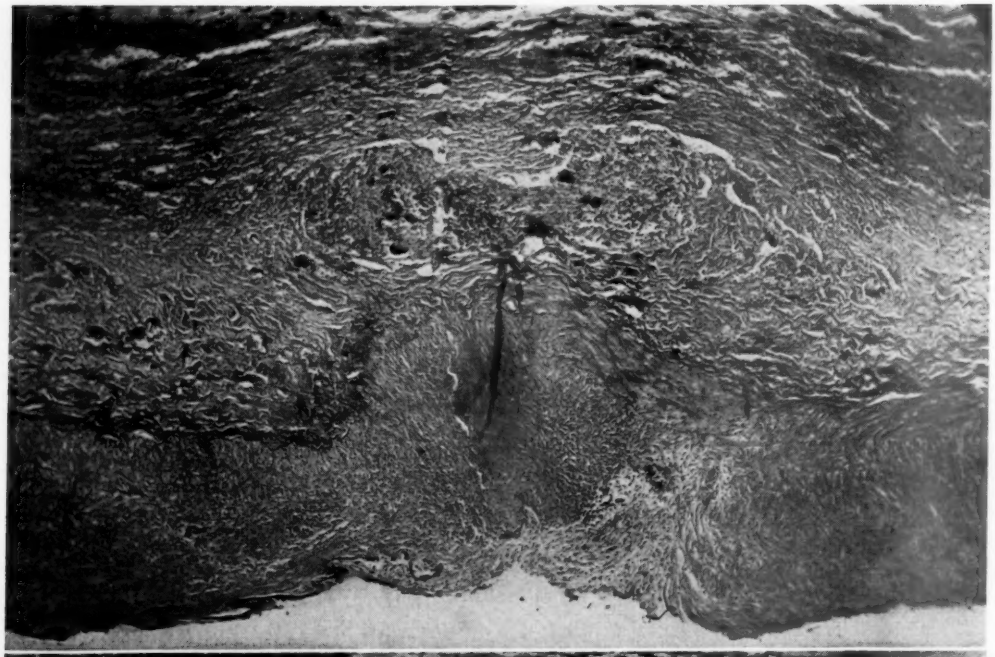


Fig. 13.

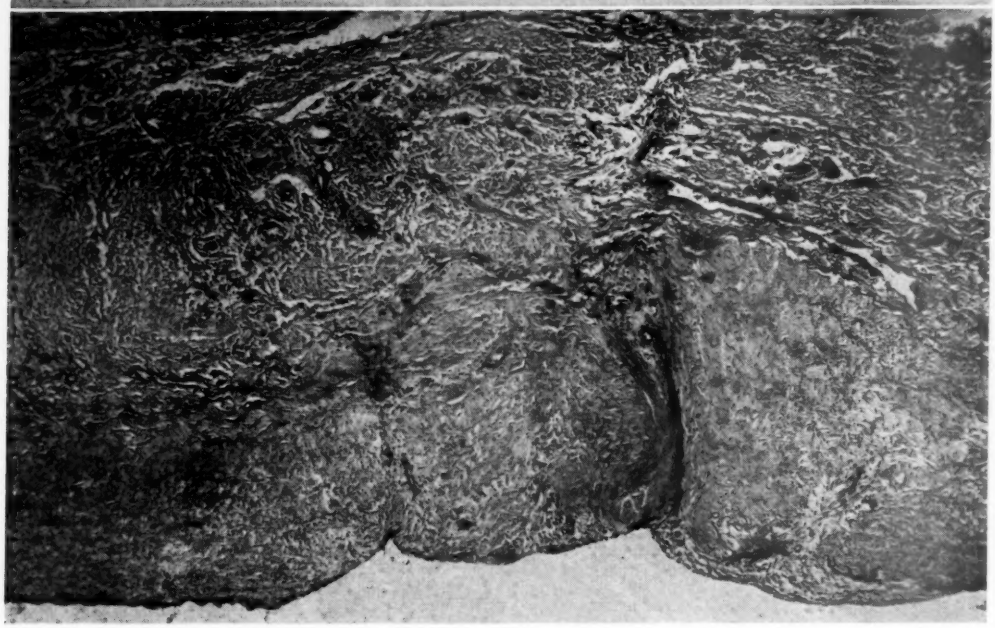


Fig. 12.—Photomicrograph of the anastomosis in a dog (11 days). Note the organization of blood clot at the suture line. The normal artery is on the left and the autograft on the right. (Hematoxylin and eosin, ×80, ¼ off reduction.)

Fig. 13.—Photomicrograph of the suture line in a dog (3 weeks). The host artery is on the left and the graft on the right. (Hematoxylin and eosin, ×80, ¼ off reduction.)

is expressed as a percentage of the normal artery (control) in Column 5 and the mean strength of the four anastomoses in each dog is found in Column 6. It is apparent that the tensile strength of the anastomoses increased with time and the sequence of events is shown in Fig. 17 which is a mean* curve of the rate in gain of strength. Tensile strength values are plotted as ordinates and the age of the anastomoses as abscissae.

Examination of the curve shows that, immediately following suture, the strength of the suture line is approximately 20 per cent of the normal artery with no significant increase in tensile strength during the following 7 to 8 days. It is clear then that during this initial phase of healing the strength of the anastomosis is dependent upon the sutures. During the following 4 to 5 weeks there is a progressive gain in tensile strength after which period there is no further significant increase.

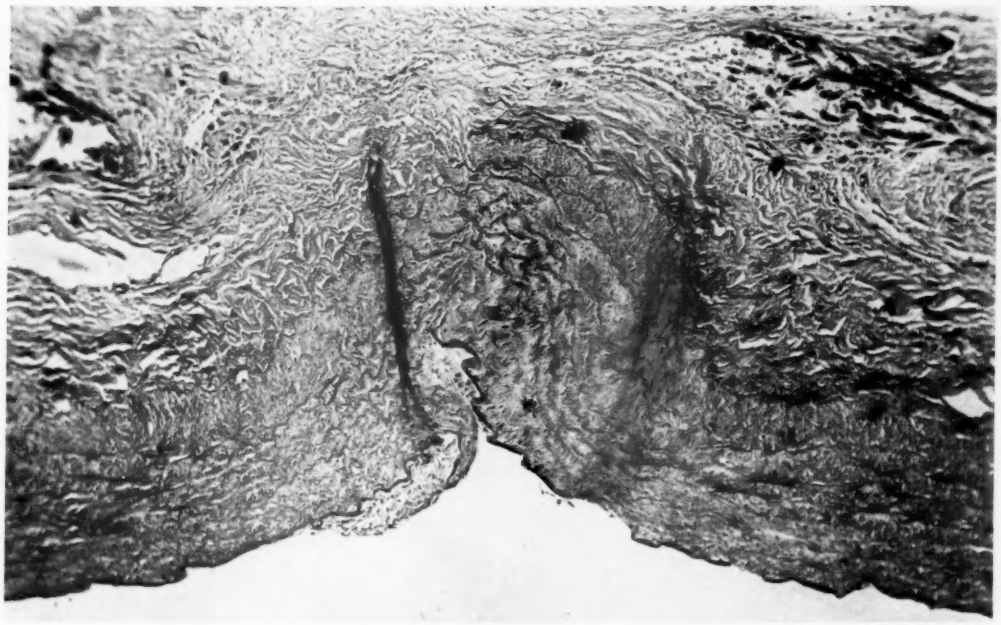
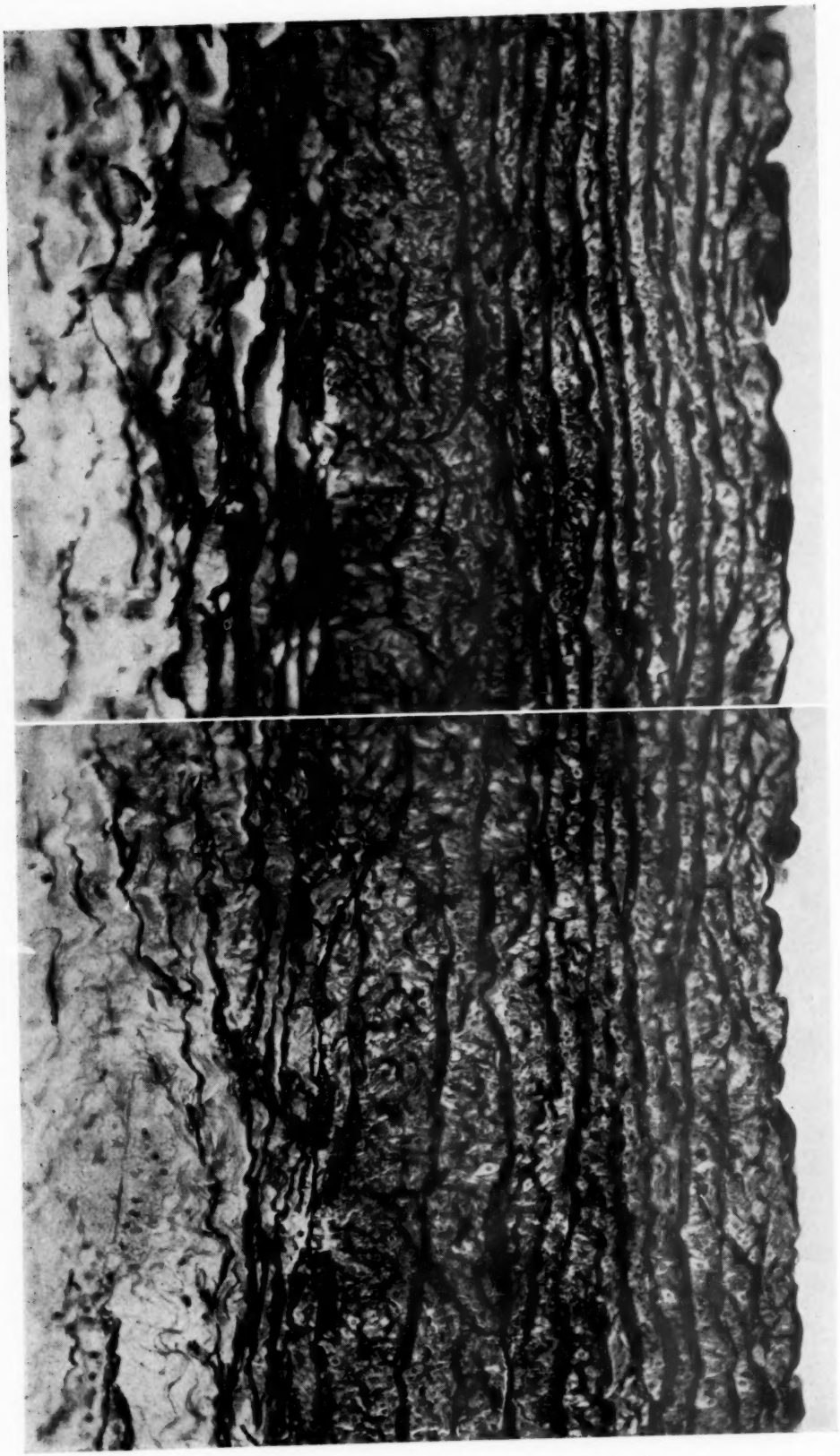


Fig. 14.—Photomicrograph of the suture line in a dog (4 weeks). In the outer half of the anastomosis, the junction is imperceptible. The normal artery is on the left and the graft on the right. Note the small mural thrombus and suture material in the adventitia.

The shape of the curve is similar to that of healing skin wounds and consists essentially of two parts, a "latent" or "lag" period followed by a period of gain in tensile strength which eventually levels off as healing becomes complete. There are, however, significant differences in the velocity of healing. While a sutured skin wound attains maximum tensile strength in approximately 10 to 14 days, maximum strength in a host-autograft arterial anastomosis occurs only after 5 to 6 weeks. Furthermore in a skin wound, the latent period is 3 to 5 days but the corresponding period in the autograft anastomoses is 7 to 8 days. It is noted that the final strength of the anastomoses is only 70 per cent

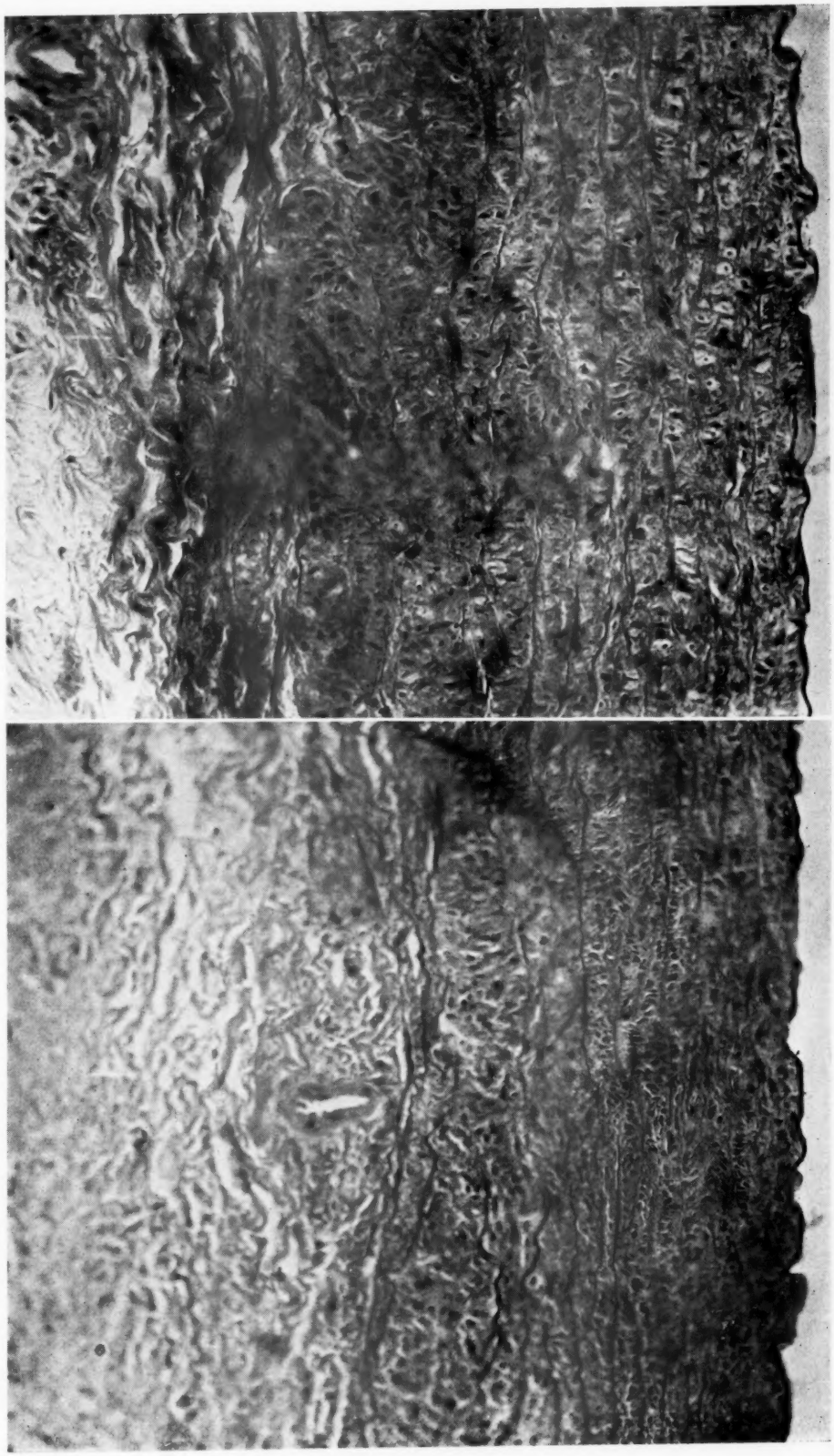
*The curve was produced by the method of least squares.[9]



B.

A.

Fig. 15.—Photomicrograph of section of host artery (*A*) and graft (*B*) taken approximately 1 to 2 mm. from the suture line in a dog (6 weeks). (Wiegert, ×250, ⅓ off reduction.)



B.

A.

Fig. 16.—Photomicrograph of the host artery (*A*) and the graft (*B*) of a dog (42 days) taken approximately 1 to 2 mm. from the suture line. (Hematoxylin and eosin, (*A*) ×125 and (*B*) ×250, ¼ off reduction.)

of the strength of the normal artery. "Final" is used with some reservation because the end point of this experiment was carried only to 56 days and the curve still shows a slight upward trend, but this is probably not significant. Lowenberg and Shumacker[8] in their study on the rate of healing of arteries repaired by end-to-end anastomosis found a curve of healing similar to that obtained for wounds of other tissues. From a study of their mean curve, the tensile strength reached a maximum after approximately 10 to 14 days.

The delay in the rate of healing of autografts as shown in this experiment can probably be explained on the basis of deficiency in local blood supply. In an artery that has been repaired by direct anastomosis, the blood supply of the artery is little compromised, unless mobilization of the vessel has been extensive. Healing can thus proceed normally. In contrast, healing in an autograft is slowed by the time required for the acquisition of a blood supply from the surrounding tissues. This contention is supported by the observation that in some of the early host-autograft anastomoses hyperemia of the intima was evident on the host side of the suture line, while on the graft side of the anastomosis the intima appeared pale. When the anastomoses were pulled apart during testing, separation always began at the entrance point of the sutures and more frequently on the graft side of the suture line. This apparent decrease in the suture holding power of the autograft would seem to indicate that the graft was weaker than the normal artery. The tensile strength of 5 autografts was tested and compared with their corresponding normal arteries and on the basis of this small number of observations there were no significant differences. In two instances, the strength of the autograft was greater than the normal artery.

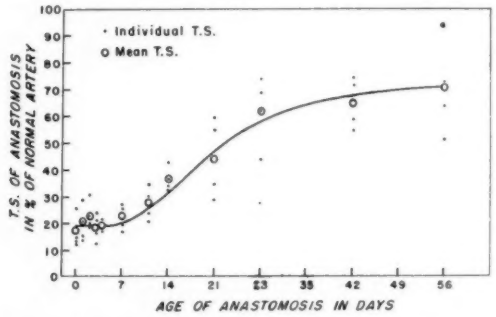


Fig. 17.—Curve of gain in tensile strength. The tensile strength of the individual anastomoses in each dog is indicated by the dots. The circle represent the mean of the 4 anastomoses in each dog.

The curve of the rate of healing obtained here is of questionable validity because of the small number of animals studied. This curve probably is not far from a true mean curve, however, because its shape resembles the curves obtained in wound healing experiments with greater statistical validity without major discrepancies in the observed values.

It has been mentioned earlier that the autografts were not tested immediately after removal from the dog and that they were stored at low temperatures for varying periods. In a previous study we found that low temperatures did not alter the tensile strength of arteries,[4] neither did the duration of deep freezing. Hallen and Gustaffson (1955)[6] also reported that low temperatures

had no effect on the tensile strength of arteries. In the event that deep freezing did alter the tensile strength, the results would have been the same, because both autograft and the normal artery were subjected to the same conditions, and the tensile strength of the former was expressed as a percentage of the latter.

The Relationship Between Tensile Strength and Wound Swelling During Healing.—Although a healing wound has a latent or lag period, this description is applied in the sense that during this phase there is no apparent increase in tensile strength. However, far from being quiescent, this period of healing is characterized by marked cellular and biochemical changes. Histologically there is hyperemia and exudation of fluid and cells. This is associated with an increase in mucopolysaccharides and the soluble protein precursors of collagen.[4] The accumulation of these elements manifests itself as swelling, which is clinically apparent in recent wounds. It had occurred to us that if the degree of swelling at the anastomoses could be measured, it would be of interest to observe whether there was any correlation between the rate and extent of its formation and the gain in tensile strength. A method to quantitate swelling presented itself readily, for in calculating the tensile strength in force per unit area the thickness of each segment of anastomosis had to be recorded. Table II shows these values at various intervals (Column 3) and they are expressed as a percentage of the thickness of the wall of the normal artery in Column 5. The

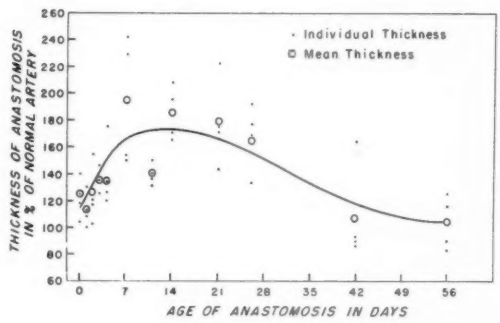


Fig. 18.

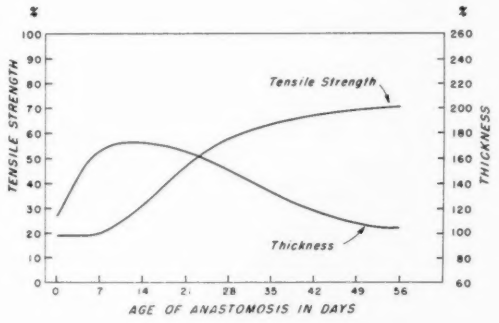


Fig. 19.

Fig. 18.—Curve to show the thickness of the anastomosis with time. The thickness of each anastomosis is indicated by the dots, and the circles represent the mean thickness of the 4 anastomoses in each dog.

Fig. 19.—Superimposed curve of tensile strength and anastomosis thickness. Note the more or less inverse relationship.

data are plotted to form a curve (Fig. 18) with percentage thickness as ordinates and age of anastomosis as abscissae. The thickness of the segments of anastomoses in some of the dogs varied widely. This is not surprising because it was not possible to remove precisely the same amount of periarterial tissue from all the arteries. Although the curve drawn is rather arbitrary due to a wide scatter of points there are some observations of interest. During the latent period of healing, there is a rapid increase in the thickness of the anastomoses which reaches a maximum about the time when the anastomoses begin to increase in tensile strength. When the tensile strength approaches a maximum, the thickness of the anastomoses decreases, finally returning to normal levels. The sequence of events is better appreciated in Fig. 19 in which the two curves are

TABLE II. THE THICKNESS OF THE ANASTOMOSES AND CORRESPONDING NORMAL ARTERIES

DOG NUMBER	AGE OF ANASTOMOSIS (DAYS)	THICKNESS OF ANASTOMOSIS (INCHES)	THICKNESS OF NORMAL ARTERY (INCHES)	THICKNESS OF ANASTOMOSIS (PER CENT OF NORMAL)	MEAN THICKNESS OF ANASTOMOSES (PER CENT OF NORMAL)
0	0	0.038	0.032	118.75	125.03
		0.038	0.027	140.74	
		0.040	0.032	125.00	
		0.037	0.032	115.62	
1	1	0.034	0.030	113.33	113.25
		0.035	0.032	109.38	
		0.036	0.036	100.00	
		0.043	0.033	130.30	
2	2	0.028	0.023	121.74	126.38
		0.034	0.029	117.24	
		0.034	0.022	154.55	
		0.028	0.025	112.00	
3	3	0.040	0.032	125.00	136.88
		0.044	0.031	141.94	
		0.050	0.037	135.14	
		0.048	0.033	145.45	
4	4	0.030	0.025	120.00	135.27
		0.036	0.030	120.00	
		0.035	0.020	175.00	
		0.029	0.023	126.09	
10	7	0.058	0.024	241.67	193.95
		0.055	0.024	229.17	
		0.049	0.032	153.12	
		0.041	0.027	151.85	
11	11	0.050	0.038	131.58	139.56
		0.049	0.035	140.00	
		0.042	0.028	150.00	
		0.041	0.030	136.67	
9	14	0.050	0.024	208.33	185.24
		0.047	0.024	195.83	
		0.043	0.026	165.38	
		0.048	0.028	171.43	
8	21	0.042	0.029	144.83	178.64
		0.043	0.025	172.00	
		0.042	0.024	175.00	
		0.049	0.022	222.73	
5	28	0.046	0.026	176.92	167.96
		0.042	0.025	168.00	
		0.035	0.026	134.62	
		0.050	0.026	192.31	
7	42	0.046	0.028	164.29	108.43
		0.027	0.029	93.10	
		0.026	0.030	86.67	
		0.026	0.029	89.66	
6	56	0.026	0.031	83.87	104.22
		0.042	0.036	116.67	
		0.044	0.035	125.71	
		0.029	0.032	90.62	

The thickness of each anastomosis is expressed as a per cent of the normal artery (control) in Column 5. The mean thickness of the four anastomoses is found in Column 6 in chronological order.

superimposed. This shows a more or less inverse relationship between tensile strength and anastomosis thickness which is consistent with the hypothesis that: (1) the anastomoses begin to gain in tensile strength when they are at their thickest. Since it has been shown by Dunphy and associates[4] that increasing tensile strength is paralleled by increase in collagen deposition, this stage of maximum thickness would appear to be the point at which collagen begins to be laid down. (2) Complete healing, at which point maximum tensile strength is reached, has occurred when the arterial wall at the site of anastomosis has contracted to its normal thickness.

SUMMARY

1. The rate of healing of arterial autografts was investigated by measuring the rate of gain in tensile strength at host-autograft anastomoses. Twenty-four fresh carotid autografts were implanted in dogs for periods varying for 0 to 56 days. Forty-eight anastomoses were studied. The shape of the curve of healing was similar to that obtained for healing wounds in general but the velocity of healing was considerably protracted. The anastomoses attained a maximal tensile strength of 70 per cent of the normal artery (control) after 5 to 6 weeks. The reasons for the delay in healing are discussed.

2. The extent and rate of tissue swelling at the healing anastomoses were measured. The curve obtained shows a more or less inverse relationship with the curve for the gain in tensile strength. This observation suggests that measurement of the diminution of swelling in a healing wound may be used as an index of the rate of healing.

3. Twenty-three of the twenty-four autografts were patent (96 per cent). In none of the patent grafts was there any evidence of stenosis, dilatation, aneurysm formation, or suture line disruption. Grossly and microscopically the autografts resembled the host artery.

We wish to express our thanks to Miss M. Schranze, S.M., and Professor P. Backer of the Department of Mechanical Engineering, Massachusetts Institute of Technology, for their help and advice with the tensile testing.

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DISCUSSION

DR. CORVESE.—The Instron type of tensiometer which was used in this work has also been used by Harrison to determine the tensile strengths of synthetic prostheses and the method is well suited to studies of this nature. Further studies are in progress to determine the rate of healing of arterial homograft-host artery anastomoses in the dog and it will be interesting to compare these healing curves with those of the autograft anastomoses.

CLINICOPATHOLOGIC OBSERVATIONS ON THE FATE OF ARTERIAL FREEZE-DRIED HOMOGRAFTS

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WE INTEND to report at this time the clinical results and the pathologic findings in our series of homografts and to attempt to make such correlations as are possible on the basis of our relatively small number of recovered grafts.

CLINICAL RESULTS

We are reporting the first 525 grafts placed in the abdomen and in the lower extremity for both occlusive and aneurysmal disease (Table I). Of these, 31 were initially unsuccessful. These are patients in whom the graft did not function because of inadequate runoff. Four of these were abdominofemoral and 27 were femoropopliteal. Most of these represent critical legs, frequently in patients with diabetes in whom we are attempting to avoid amputation despite the presence of unsuitable outflow. These could be eliminated in the future by closer selection of patients but in view of the present salvage rate in grafting pregangrenous limbs, we feel that this incidence of primary lack of success is justified.[1] This group does not include those patients who developed an immediate postoperative thrombosis, the so-called "take-backs." During the first year of grafting we found that we were taking back to surgery one of every 4 grafts to remove soft clots and to generally dress up the toilette of the graft before it would function properly. To try to minimize this we began several years ago to use noradrenalin (Levophed) routinely to maintain a patient's systolic pressure at whatever level was necessary to procure conclusive pulses in the proper locations below the graft. Since then we have had to reopen only 3 of the last 400 grafts.

Table I

Total operated cases	525
Primarily unsuccessful	31
Deaths	
Due to technical failure	4
Due to homograft failure (6 with infection)	10
Due to other cause (14 ruptured aneurysms)	42
Total available for follow-up	438
Total late shutdowns	70
Total remaining successful	368

Read at the Twelfth Annual Meeting of the Society for Vascular Surgery, San Francisco, Calif., June 22, 1958.

There was a total of 56 deaths. Four of these patients died through technical failure of an inadequate proximal anastamosis in aneurysm. Ten others died through failure of the homograft itself. Six had local infections with resultant rupture of the graft. Two others died from erosion of the homograft as it pulsated against the cut end of the patient's own calcified vessel. Two died from rupture of a saccular aneurysm. The other 42 died due to causes associated with major surgery but not specifically a graft. These included, for the most part, deaths due to myocardial infarction, rhythmic changes in the heart, usually ventricular fibrillation, and cerebral anoxia. Renal failure has been prominent in the patients with aneurysms who have bled to some degree prior to surgery. A thrombocytopenic hemorrhagic diathesis has caused death in some of the patients with aneurysms who had bled a great deal prior to surgery and who required massive transfusions.[2] This has recently been found to be correctible by direct transfusion through siliconized equipment. Thirteen have died since the time of grafting from various causes, seven of them with associated cardiovascular disease. A total of 438 patients are available for follow-up study. Of these, 70 have incurred some incident in their postoperative course that has resulted in the loss of distal pulses and a presumed failure of the graft. Three hundred and sixty-eight remain successful for periods ranging up to 4½ years.

The only cases to be discussed at the present time are the 70 in whom late shutdown has occurred. Five of these grafts were lost through primary wound infections in the leg. This combined with the 6 fatalities due to infection makes a total of 11 infections, or 2 per cent. This rather high rate is perhaps partially explained by the poor nutrition of these limbs and their inadequate resistance to infection. We have found that in the presence of infection with associated proteolytic digestion of the homograft, the only safe procedure is to remove the graft, tie off the patient's own vessels, and abandon the project.

Thirty-five of the late shutdowns have not been regrafted. Four of these patients had sufficient symptoms to warrant a regraft but refused further surgery. The remaining 31 are symptom free or have attained sufficient benefit from the original procedure, cause unknown, to be content with their situation as of the time of the late shutdown. This leaves 30 of the late shutdowns who were redone. Two of them were initially unsuccessful, two have suffered a second late shutdown, and the remaining 26 are still patent and functioning.

The distribution of the late graft shutdowns is interesting (Tables II and III). Most are in the femoropopliteal area due to the smaller caliber of vessel. The sudden decrease beginning with 1957 is directly related to a change in technique which has lowered the number of late shutdowns to a significant degree. In both elective and nonelective cases it will be noticed that there have been no late shutdowns in the group done for aneurysm. We believe this is quite significant. Also of significant clinical interest is the time of shutdown following a graft (Fig. 1). The great bulk of shutdowns occurred within the first year. If a graft manages to survive the first year, the chances of late shutdown become less as time goes on.

TABLE II. LATE GRAFT FAILURE—ELECTIVE

YEAR	TOTAL	AORTOILIAC	FEMOROPOPLITEAL	AORTIC ANEURYSM
1954	25	2	4	0
1955	56	3	7	0
1956	106	4	21	0
1957	119	1	8	0
1958	55	0	0	0

TABLE III. LATE GRAFT FAILURE—NONELECTIVE

YEAR	TOTAL	AORTOILIAC	FEMOROPOPLITEAL	AORTIC ANEURYSM
1954	5	0	1	0
1955	27	0	1	0
1956	45	4	6	0
1957	58	1	7	0
1958	29	0	0	0

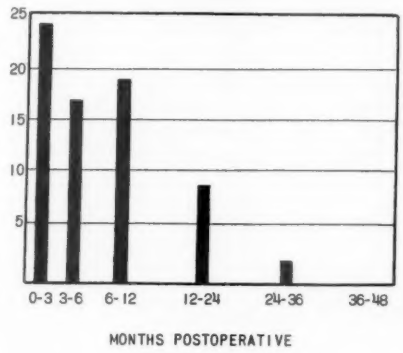


Fig. 1.—Late shutdown. Time of occurrence.

PATHOLOGIC FINDINGS

We can report the pathologic findings in only 33 instances. Thirty grafts were obtained from regrafting and three others were obtained from late deaths. There have been 6 types of pathologic change seen in the homografts.

1. Arteriosclerosis has occurred in 7 of the grafts recovered (Fig. 2). None of these have developed arteriosclerosis to the point where it was of clinical significance.

2. One case developed multiple aneurysmal dilatation (Fig. 3). This represents spread in a suture line which ran down the longitudinal axis of the graft.

3. One case of arteriosclerotic aneurysm has occurred (Fig. 4) in a femoral graft. This ruptured into the thigh at 9 months and was replaced.

4. Four cases of saccular aneurysm have developed. Careful pathologic study of multiple sections has not revealed the cause for the development of such an aneurysm although the question of local proteolysis due to areas of infection is under consideration (Fig. 5). Two of these have been regrafted, one because of rupture into the thigh and one because we feared rupture. The other two occurred in the abdomen and were the cause of two of the deaths.

Fig. 2.

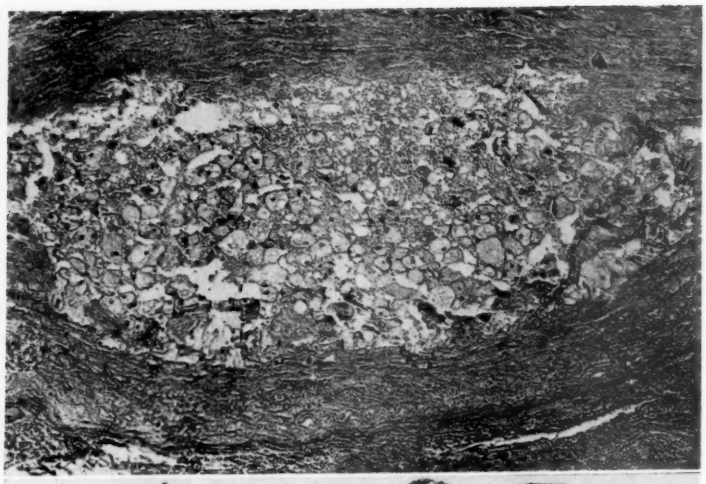


Fig. 3.

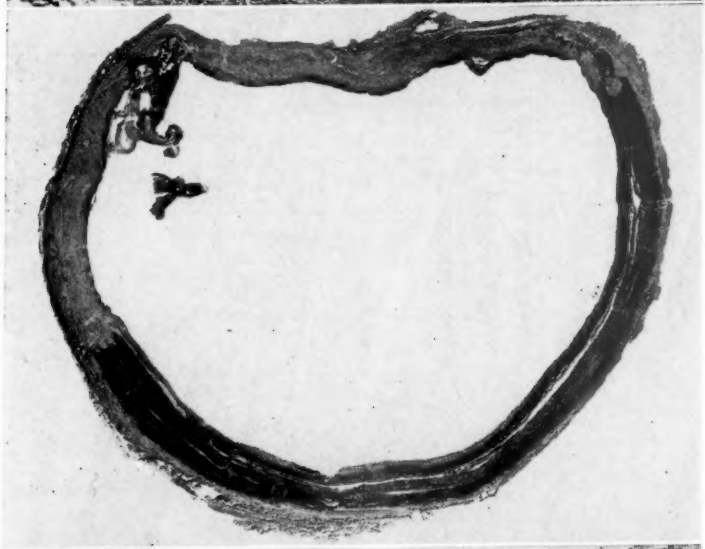


Fig. 4.

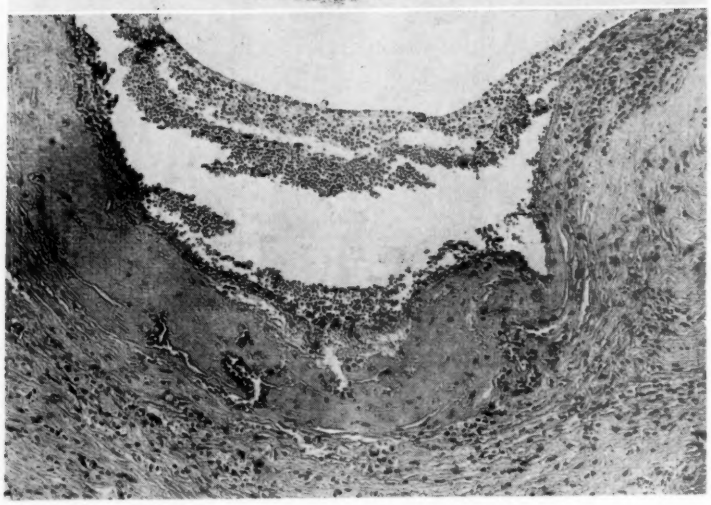


Fig. 2.—Localized collection of lipophages within media forming an early atheroma. (Hematoxylin, eosin, and methylene blue, × 50.)

Fig. 3.—Verhoeff's elastic stain shows a defect in the continuity of the elastic fibers of the media in the upper half of the arterial wall. The gap has been bridged by collagen supplied by the host. (× 5.)

Fig. 4.—Arteriosclerotic aneurysm in homograft at 9 months. Marked thinning of homograft wall with extensive lipophage infiltration. Special stains show sparse elastic fibers. (Hematoxylin, eosin, and methylene blue, × 80.)

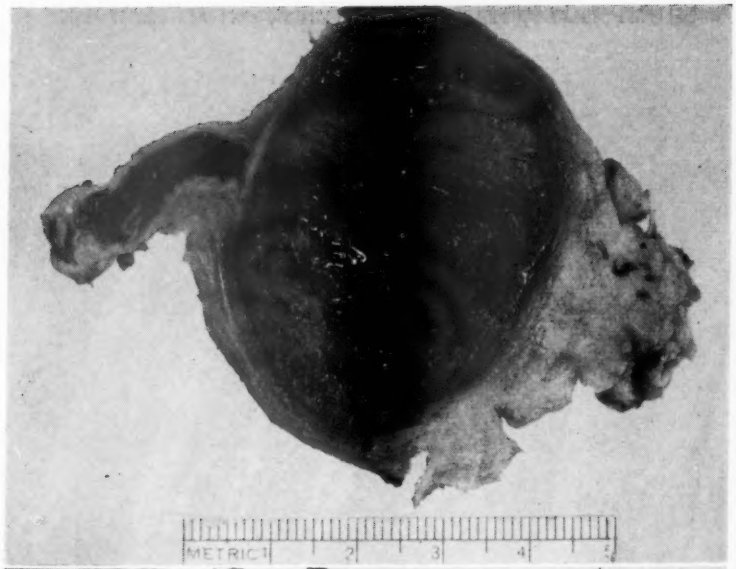


Fig. 5.

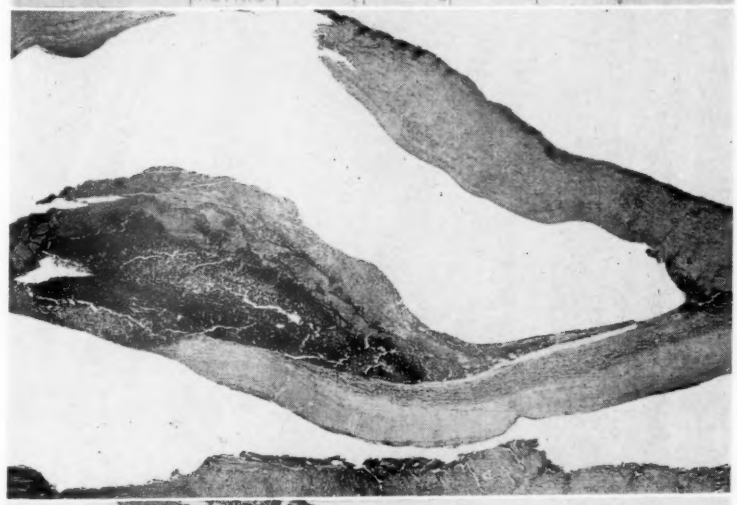


Fig. 6.

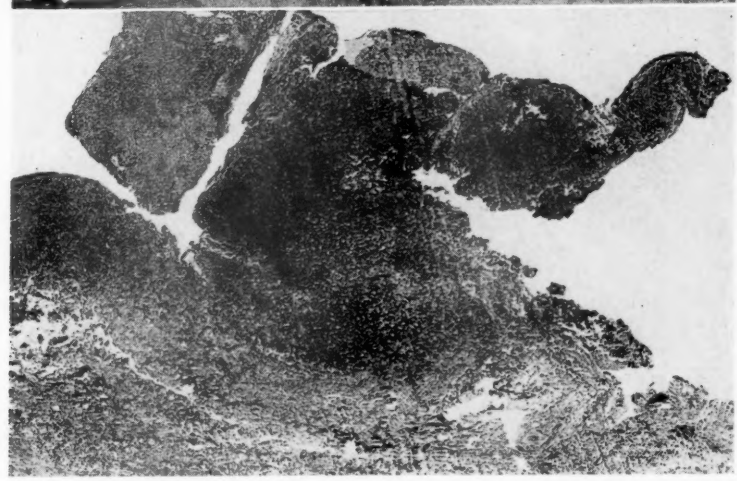


Fig. 7.

Fig. 5.—Saccular aneurysm of femoral artery homograft at 9 months postoperative.

Fig. 6.—The media is seen to be split at the point of dissection. The intimal defect is seen in upper right portion of the figure. (Hematoxylin, eosin, and methylene blue, × 8.)

Fig. 7.—Section shows heavy purulent exudate about homograft with defect through the entire thickness of wall. (Hematoxylin, eosin, and methylene blue, × 30.)

Fig. 8.

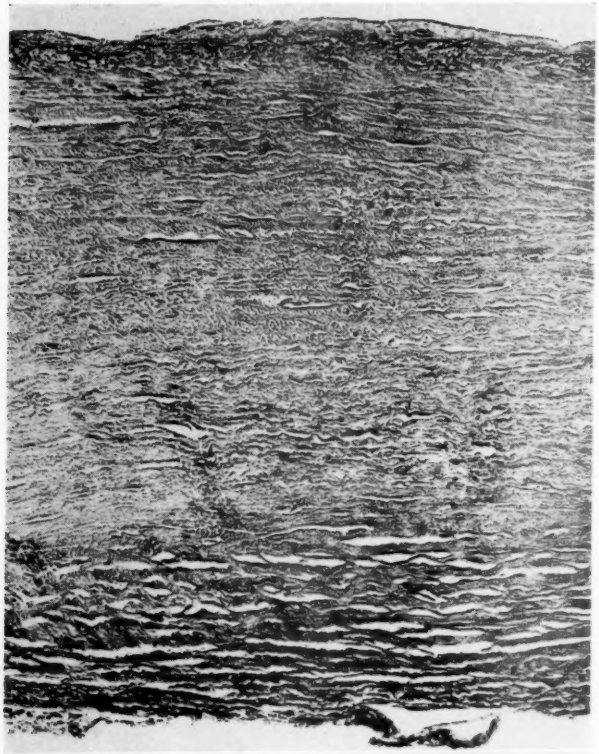


Fig. 9.

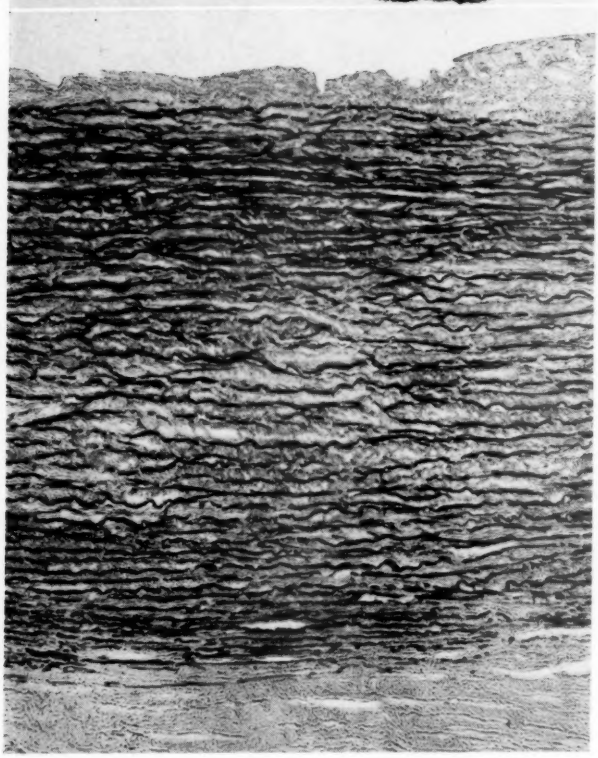


Fig. 8.—Masson stain on 22-month-old homograft shows good retention of collagen within the media. (× 80.)

Fig. 9.—Verhoeff's elastic tissue stain shows well-preserved elastic fibers in media and in approximately normal numbers. (× 80.)

5. One dissection occurred within a graft (Fig. 6). This caused a sudden occlusion and was regrafted. The cause of the local dissection could not be ascertained.

6. Finally, there are the 11 instances of rupture due to infection (Fig. 7).

The remaining homografts and the portions of the preceding ones unaffected by the local change were grossly and microscopically quite satisfactory (Figs. 8 and 9). The collagen holds up well, the elastica is only slightly fragmented, and capillaries have grown through the graft to the outer one-half of the media.

A. *B.*

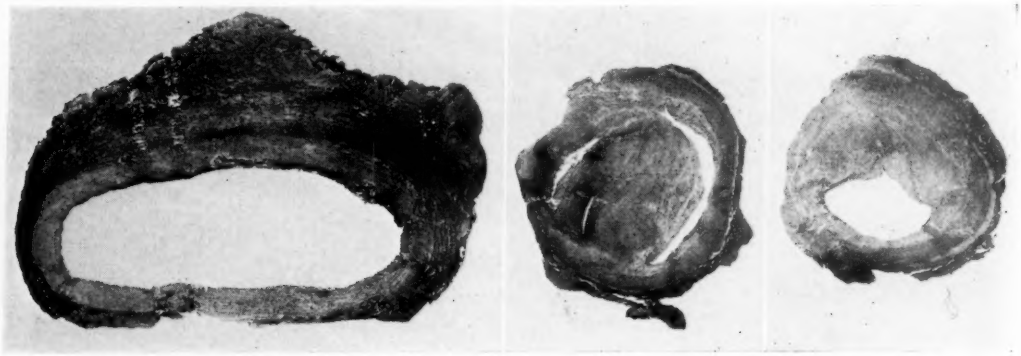
Fig. 10.—*A*, Original femoral arteriogram, superficial femoral artery occlusion from the common femoral bifurcation to mid-Hunter's canal. *B*, Femoral arteriogram renewing late shutdown, superficial femoral artery occlusion from the common femoral bifurcation to mid-Hunter's canal.

A different point of view is obtained if these recovered grafts are evaluated in terms of their clinical significance (Table IV). One late shutdown was due to arteriosclerosis present in the homograft at the time of implant. One was due to an arteriosclerotic aneurysm. One was due to local dilatation in a graft which had a longitudinal suture line from having converted a thoracic aorta into a smaller tube. Two had saccular aneurysms. The remaining 28 shutdowns were shown conclusively to be due to progression of the patient's basic arteriosclerotic disease rather than to any fault within the homograft itself.

TABLE IV. LATE OCCLUSION IN THE 33 GRAFTS RECOVERED AT REOPERATION AUTOPSY

Progression of patient's basic disease—Arteriosclerosis	28
Arteriosclerosis in homograft	1
Arteriosclerotic aneurysm of homograft	1
Aneurysmal dilatations of homograft due to expansion of longitudinal plication	1
Saccular aneurysm (1 with rupture)	2
Total	33

Fig. 10 illustrates a typical case. The original segmental occlusion of the superficial femoral artery extended from the femoral bifurcation to mid-Hunter's canal. Nine months postgraft the patient experienced a sudden shutdown of the homograft. A new angiogram showed an area of occlusion extending from the femoral bifurcation to the femoropopliteal junction. Fig. 11 illustrates cross-sections above, at, and below the distal anastamotic line. The graft itself was, of course, filled with soft clot. At the femoropopliteal junction the patient's own vessel was again of normal caliber and a graft to this new location was done.



A. *B.* *C.*

Fig. 11.—*A*, Cross-section of homograft one inch proximal to the distal anastomosis line. The soft clot present in the graft at the time of surgery has been lost in processing. (Hematoxylin and eosin, × 7.) Cross-section of patient's own femoral artery one inch (*B*) and two inches (*C*) distal to the distal anastomosis line. This degree of arteriosclerosis was not present 9 months earlier. (Hematoxylin and eosin, × 7.)

Fig. 12.—Aortogram made 47 months following an aortic bifurcation homograft.

Whether the trauma of surgery and the stimulus of healing in the region of an anastamotic line speeds up the development of arteriosclerosis is a subject for conjecture.

We do not routinely follow patients with periodic angiograms, but those few which have been done have been quite satisfactory in appearance. Fig. 12 shows such an angiogram done 47 months after an aortic bifurcation graft.

CORRELATION OF CLINICAL RESULTS AND PATHOLOGIC FINDINGS

Few dogmatic statements may be made by correlating the clinical results with the pathologic findings, but some general impressions have arisen.

Although a homograft is subject to many of the diseases of the original vessel for which it is substituted, in our experience, the incidence of these faults has been low and the clinical significance of the changes even less. In connection with this, x-ray screening of grafts, postprocessing, has been useful in preventing the introduction of pre-existing arteriosclerosis (Fig. 13).

When a homograft becomes infected the only safe course to follow is to remove the entire graft and abandon the project.

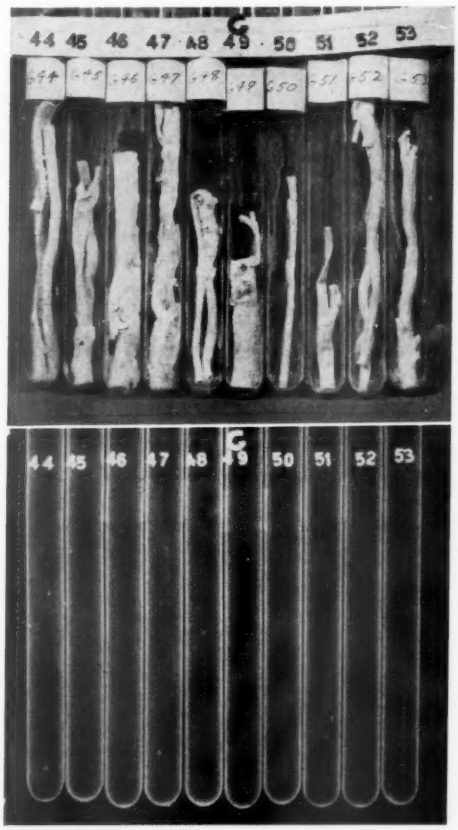


Fig. 13.—The x-rays in the lower half of the figure match the grafts in the upper half. Grafts G-48 and G-51 show objectionable calcification and should be discarded.

The postoperative death rate from other manifestations of arteriosclerosis once the patient has been released from the hospital is low (1.3 per cent), but the immediate postoperative death rate from other arteriosclerotic manifestations, particularly as related to the heart, comprises approximately 5 per cent of the total grafted patients.

The incidence of primarily unsuccessful grafts may be minimized by the use of several devices. These are generally not necessary when one is inserting abdominal grafts since these almost always do well. However, when one does femoral grafting, particularly in the critical leg, the importance of these devices

becomes increasingly great. These are: (a) the use of arteriography of diagnostic quality so that the outflow may be evaluated as well as possible, (b) the use of noradrenalin (Levophed) to maintain adequate pulses in the proper locations distal to the graft over the first few days by elevating the systolic pressure, and (c) the use of a mechanical device, in evaluating the outflow in questionable patients (Fig. 14), through which blood may be pumped at known volume and pressures into the popliteal artery of the patient prior to putting in the graft. If an adequate amount of blood is accepted by the patient at a systolic pressure that is reasonable, we go ahead with the graft. If distal resistance is too high to permit a proper volume of blood at a reasonable pressure, we abandon the procedure at this point since we know that it will be primarily unsuccessful.

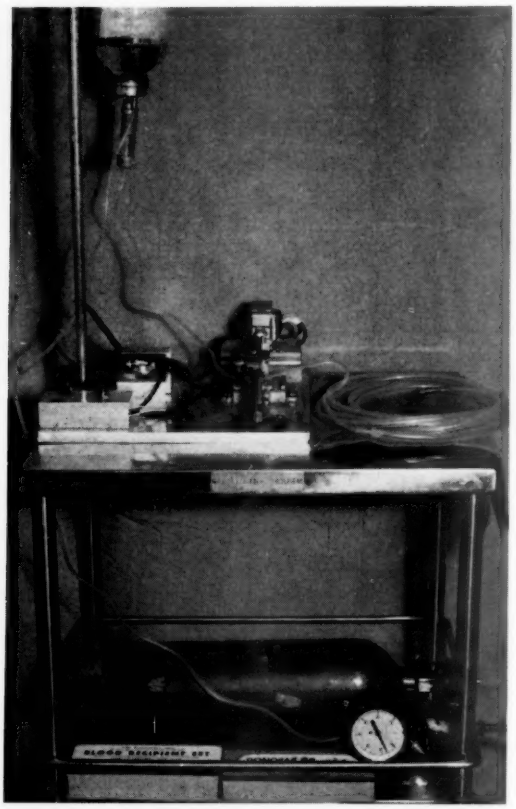


Fig. 14.—Blood from the upper reservoir is passed through tubing to the patient's femoral or popliteal artery. Pressure is supplied from an oxygen tank below. Intermittency of flow is produced by periodically releasing a clamp through which the tubing passes. This is regulated by a cam-driven timer and an electromagnet activated by a simple solenoid.

A total of 70 grafts have now shutdown over varying periods of time during the last 4½ years. Of these, 15 were aortoiliac and 55 were femoropopliteal—this is in direct relation to the size of the vessel. All of these were in patients with occlusive disease. We have yet to see a late shutdown in a patient with aneurysmal disease. Since the bulk of late shutdowns are due to advancement of the basic occlusive disease it is not surprising that grafts

for aneurysm do not shut down if the graft material used is satisfactory. Although in occlusive disease more vessels shut down as time goes by, the frequency of shutdowns becomes less as time progresses (Fig. 1). Perhaps some patients have an inherently more "active" disease which progresses rapidly following surgery to produce a second occlusion in a short time. Others are not acutely progressive and can be expected to go for much longer periods of time before further occlusion occurs.

CONCLUSIONS

We may expect long-standing good results in those patients with aneurysm who survive their surgery. We may also expect a certain acceptable percentage of late shutdowns in occlusive disease, not necessarily of clinical importance, more in femoropopliteal than in aortoiliac grafts, which is in direct proportion to size of vessel, to degree of "activity" of disease, and undoubtedly to other, as yet unknown, factors. However, the longer a graft remains functional, the better the chances are that it will continue to remain functional.

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DISCUSSION

DR. JERE W. LORD, JR. (New York, N. Y.).—Dr. Lazzarini and I have carried out studies over the past 2 years, on the immunologic reaction of aortic homografts and plastic prostheses made of Dacron. These studies have been performed in 4 patients of each group who have had the grafts and prostheses inserted over a period of 3 years to 1 year. An antigen was made from human aorta and injected intradermally. Positive reactions were noted in all patients with aortic homografts whereas no reaction was observed when aortic antigen was injected into those with Dacron prostheses. In contrast, an antigen made of Dacron prosthesis was nonreactive in both groups of patients. We wonder if this immune response may account for some instances of failure of aortic homograft. We have observed two late thromboses 2 years after successful function for over 23 months.

It is also an interesting possibility to speculate on whether or not the insertion of a second arterial homograft following failure of the first would not lead to an accelerated immune response and therefore to higher incidence of failure in this group than one would expect from the disease process for which the graft is inserted. I wonder if Dr. Humphries has noted this in his recent second series of homograft implantations.

DR. OSCAR CREECH, JR. (New Orleans, La.).—It has been demonstrated convincingly by Lansing that the process of atherosclerosis consists of deterioration of the elastic components of the arterial wall followed by deposition of lipids. He has suggested that breakdown and calcification of medial elastic tissue probably precedes atheroma formation and may be related to the decrease in production of elastase by the pancreas.

In the preserved arterial homograft, although the elastic fibers persist for long periods of time, this structural element eventually deteriorates and it has been our observation and the observation of others that when this occurs atheroma formation in the homograft is likely to occur. The homograft, no matter how it is processed and preserved, does not survive intact and therefore represents an area of injury in the arterial system. Thus the circumstances are such that the formation of atheromas is a natural consequence.

DR. D. EMERICK SZILAGYI (Detroit, Mich.).—I would like to bring to your attention some of the histological aspects of the behavior of the arterial homografts on which Dr. Humphries did not have enough time to dwell.

About a year and a half ago we critically surveyed the late results of our arterial homografts in 270 clinical cases and examined histologically 28 grafts recovered at autopsy or secondary operations. Our findings contradicted some suppositions that had been generally accepted earlier. We found that, with very few exceptions, arterial homografts are not truly accepted and incorporated by the host tissues. They are invested by a thin connective tissue shell but otherwise as a rule they are merely biologically stored. Thus the ultimate fate of an arterial homograft depends upon its original structural characteristics. Moreover, the only histologic element of the graft that survives is the elastic tissue, and when this wears out the graft begins to show structural changes. The durability of a homologous arterial implant can be influenced to some degree by choosing homografts of excellent quality which, all other things being equal, will last longer; undoubtedly the grafts Dr. Humphries used were such. In general, however, the decisive factor is the fundamental histologic structure of the graft which, of course, is immutable. The femoral artery is very poor in elastic elements and usually it wears out quickly. In our experience the structural derangement becomes common after 2 years of implantation and in 3 years only about one-third of the implants appear intact in angiograms. The aorta, which is extremely rich in elastic tissue, fairs much better. As a matter of fact, I believe in most, but by no means all, instances the aortic graft outlasts the patient. In aortoiliac grafts the iliac limbs of the implant, which are intermediate between the aorta and the femoral artery insofar as their elastic tissue component is concerned, show relatively early changes. These circumstances raise grave concern about homografts. I believe it behooves us to watch the clinical progress of aortoiliac homografts with great care for the evidences of aneurysm formation. While the occurrence of such complications is not very common, even a low incidence of occurrence presents obvious dangers.

DR. ROBERT R. LINTON (Brookline, Mass.).—At present, I am more in agreement with Dr. Szilagyi than I am with Dr. Humphries in regard to the long-term results of homografts. In reviewing our cases, unfortunately I cannot give you the actual figures, but it is my opinion, and despite Dr. Humphries' statement to the contrary, most failures of grafting procedures of the lower extremity are the result of failure of the graft and not the progression of the patient's disease. In my experience over many years with the treatment of obliterative atherosclerosis of the lower extremities, for the most part it is a slowly progressive one and a cataclysmic sudden late occlusion of the various types of grafts would indicate to me that it is sudden occlusion of the graft which is the cause of failure rather than the slow type of occlusion one sees in the host arteries. It is for that reason I think we must look for a better type of graft than the homograft and perhaps it will be one of the newer synthetic materials. At present, I place a saphenous vein autograft as first choice in arterial reconstructive surgery, since I have not yet seen a venous autograft occlude if the graft was patent at the time of discharge from the hospital. The longest follow-up I have on this type of graft is 8½ years and this graft is still patent. I believe the next best type of arterial reconstruction is the Cannon type of thromboendarterectomy. In some cases this can be supplemented where necessary with a small segment of saphenous vein autograft. Again with this type of reconstructive surgery, one is dealing with autogenous tissue which I believe is very important. My next choice, when these two methods cannot be utilized, is the arterial homograft and my fourth is a synthetic prosthesis.

DR. HUMPHRIES (closing).—In answer to Dr. Lord's question, we too were interested in sensitivity and in the first 40 or 50 patients we did skin testing. Finding no positives we discontinued the procedure. Regarding those patients regrafted, there are 26 remaining patent of the 30 who were redone. This is a better figure by twice than those of the total series and it must be borne in mind that, because they are second grafts, they are also shorter in follow-up time. I would feel that probably they are going to end up about the same as those done only once.

I was very interested in Dr. Creech's comment. I wonder sometimes what the general milieu or environment of an artery has to do with the development of arteriosclerosis. Certainly there is more than just degeneration in an arterial wall when dead arteries and even foreign material can develop arteriosclerosis.

Because of our experiences, I, unfortunately, cannot agree with Dr. Linton's thoughts concerning the best method of grafting at present.

The slide that we showed at 42 months of a graft with the rather good elastic tissue was incidentally a femoral graft. Dr. Szilagyi showed me one year ago x-rays of femoral grafts that were becoming quite sclerotic. This was disturbing. We then arteriogrammed some of ours. Unfortunately, the follow-up is not nearly as accurate or as comprehensive as his series but those x-rays that we did take on patients up to 3 and 4 years postgrafting, particularly in the femoral area, actually looked about the same as they did when they were taken at one year. I cannot explain this difference. Perhaps our troubles are imminent, but just not here yet.

THE USE OF INTRAVENOUS PITUITRIN IN TREATMENT OF BLEEDING ESOPHAGEAL VARICES

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(From the Department of Surgery, University of Rochester School of Medicine and Dentistry)

INTRODUCTION

THE therapy of the acute bleeding from esophageal varices has had numerous and varied approaches, both surgical and nonsurgical in nature. The multiplicity of approaches which have been suggested indicates a lack of satisfaction with any single regimen and the consequent need for therapeutic additions and improvements. Surgical Pituitrin or Pitressin, administered intravenously to experimental animals, resulted in a temporary fall in portal pressure[7, 12, 13, 18] and, therefore, their use was proposed as a supplement to other methods of controlling hemorrhage from esophageal varices.[13] Our clinical experience suggests that these drugs are very effective in the control of the acute bleeding episode and that they are also helpful in diminishing the marked bleeding encountered during transesophageal ligation of varices. In addition to the beneficial effects noted clinically, direct measurements of portal vein pressures in patients with portal hypertension have demonstrated that intravenous surgical Pituitrin results in a significant decrease in portal pressure under these conditions.

BACKGROUND

Wiggers[36, 37] demonstrated that extract of the pituitary gland would cause diffuse vasoconstriction of the arterioles and initially suggested that it be applied to the therapy of massive hemoptysis. Rist[28] reported 12 cases in which intravenous Pituitrin stopped pulmonary hemorrhage, which could not be controlled by other methods. Trimble and associates[32] reported its use on 46 occasions in 32 patients with prompt control of pulmonary bleeding. Only the intravenous route proved consistently effective.

On the basis of the effect of the drug on pulmonary hemorrhage, Kehne and associates[13] used Pituitrin in two cases of bleeding esophageal varices and caused prompt cessation of bleeding on 5 occasions in one of the patients and on two occasions in the other patient. The pharmacologic effects of intravenous Pituitrin on the portal circulation in experimental animals have been investigated by several approaches.[7, 12, 13, 18] A prompt fall in portal venous pressure and portal flow was consistently demonstrated and attributed to a marked constriction of the arterioles of the splanchnic bed. These changes were inconsistently accompanied by a slight rise in systemic arterial pressure and a minimal alteration in systemic venous pressure. The extent of portal pressure reduction ranged

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from 20 per cent in normal animals to 49 per cent in dogs with inferior vena caval obstruction causing portal hypertension.[13] Davis and co-workers[10] studied the effect of Pituitrin in the human and in two cases with proved esophageal varices, which never bled, demonstrated a decrease in portal pressure and flow as manifested indirectly by a lowering of the intrasplenic pulp pressures and the hepatic vein wedge pressures. No changes in hepatic oxygen consumption were noted. One patient was esophagoscoped and marked blanching of the mucosa and decrease in the size of the varices were seen after the administration of intravenous Pituitrin.

METHODS AND RESULTS

Physiologic Studies.—The direct effect of intravenous surgical Pituitrin on portal venous pressure was investigated in 9 patients during operation for portacaval or splenorenal anastomosis. With the patient under endotracheal anesthesia, a combined thoracoabdominal approach was made in all patients. Most patients had been receiving cyclopropane and, one-half hour prior to injection of Pituitrin, the anesthetic agent was changed to avoid potentiating cardiac complications. A No. 19 needle was inserted into either portal or splenic vein and pressures were measured by means of a water manometer or strain gauge. After the initial pressures were recorded, 20 clinical units of surgical Pituitrin (Parke, Davis & Co.) in 200 c.c. of 5 per cent dextrose in water were given intravenously over a 4- to 9-minute period. Portal pressures were recorded for 15 minutes and the needle was removed. A final portal pressure was measured subsequent to the establishment of the proposed shunt in those cases in which an anastomosis was feasible. Simultaneous brachial arterial pressures were determined by means of a sphygmomanometer and, in 4 instances, the inferior vena caval pressures were also measured.

In 8 of the 9 patients studied, a marked and rapid decrease in portal pressure occurred subsequent to the injection of surgical Pituitrin (Figs. 1 and 2). The portal vein pressure was reduced by Pituitrin administration to the same level that resulted from a subsequent shunt when one was performed (Fig. 1, *A* through *F*). In one patient there was no apparent alteration in portal pressure after injection of Pituitrin. In only one instance was a significant arterial hypertension produced and in this case (Fig. 1, *B*) the blood pressure elevation was transitory. The vena caval pressures showed no significant alterations (Fig. 1, *B*, *D*, and *F*) and there were no untoward effects of the drug noted.

Clinical Experiences.—Intravenous surgical Pituitrin or Pitressin was used therapeutically in 11 patients with acutely bleeding esophageal varices. The estimated blood loss prior to institution of therapy varied between 250 and 1,000 c.c. Ten of these patients were alcoholic cirrhotics. The other patient's varices were secondary to thrombosis and cavernomatous transformation of the portal vein. In all instances the presence of varices was confirmed by esophagogram or esophagoscopy. A Levin nasogastric tube or an *uninflated* Sengstaken-Blakemore tube was inserted in 9 of the patients in order to maintain a constant gastric suction and thus decrease regurgitation into the esophagus of gastric fluid. Twenty clinical units of surgical Pituitrin (Parke, Davis & Co.) or Pitressin (Parke, Davis & Co.), usually diluted with 200 c.c. of 5 per cent dextrose in distilled water, were administered over a half hour period and the nasogastric tube irrigated at half hour intervals. The quality of the gastric irrigation return coupled with serial vital signs and microhematocrit determinations were used as a guide to the status of bleeding and the effect of therapy. Nonprotein nitrogen and electrolytes were checked daily and any untoward symptoms which could be related to the drugs were noted.

In the group of 9 patients, 25 distinct episodes of acute bleeding were so treated with prompt control 22 times (Table I). The gastric aspirate cleared 5 to 20 minutes after the completion of intravenous Pituitrin or Pitressin. The vital signs and microhematocrit

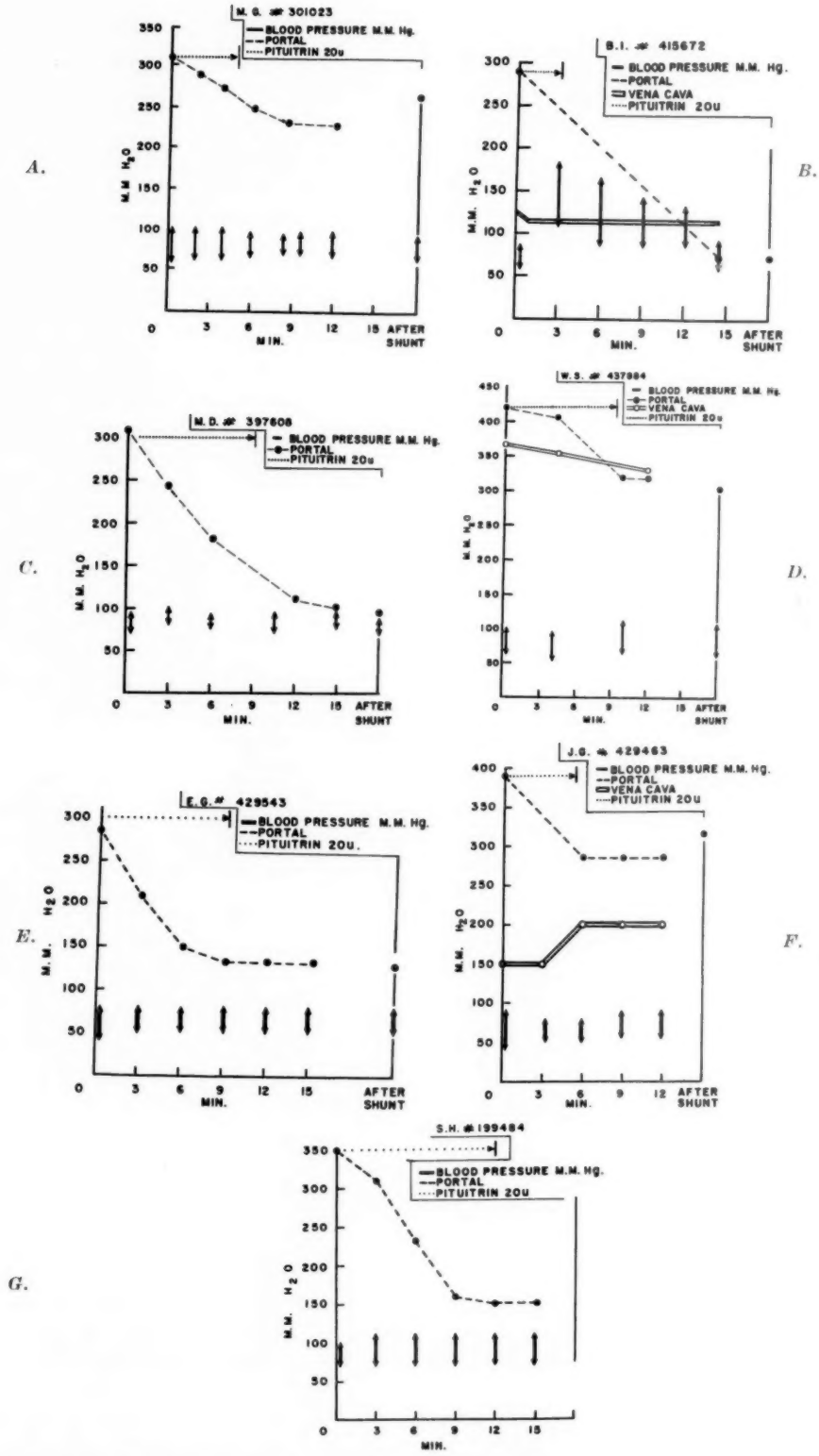

Fig. 1.—Direct measurements at operation demonstrating the effect of intravenous surgical Pituitrin on portal venous pressure, arterial pressure, and inferior vena caval pressure. Comparison between the effect of Pituitrin and portacaval anastomosis on portal pressure.

determinations showed stabilization and later improvement with transfusion. In several instances bleeding recurred after an interval of quiescence ranging from 6 hours to several days and Pituitrin was used to control the second and other subsequent episodes.

TABLE I. PITUITRIN (PITRESSIN) THERAPY OF BLEEDING ESOPHAGEAL VARICES

REGIMEN	PATIENTS	BLEEDING EPISODES	EFFECTIVE CONTROL
Pituitrin and Levin tube	5	18	16
Pituitrin and Sengstaken tube (uninflated)	4	7	6
Pitruitin after Sengstaken tube failure	2	2	2

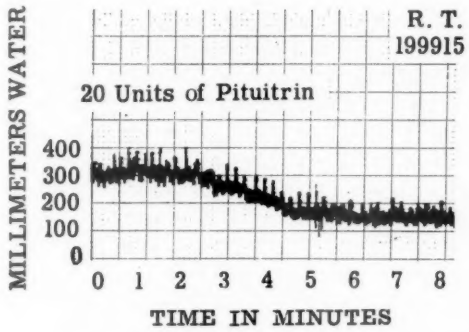

Fig. 2.—Sanborn recording of portal pressure during administration of surgical Pituitrin at operation.

CASE REPORT

R. K., SMH #429855, a 42-year-old white man, was admitted to the hospital on Feb. 5, 1957, with a one-day history of acute upper gastrointestinal bleeding. He was a known alcoholic cirrhotic and during the 6 months prior to admission he experienced two episodes of melena and hematemesis. On Feb. 9, 1957, transesophageal ligation of varices was performed and the patient was discharged after a benign postoperative course on Feb. 23, 1957. He was readmitted the following day with melena and on Feb. 26, 1957, a portacaval shunt was performed. The procedure was technically difficult and it was felt that the shunt functioned poorly if at all. Three days postoperatively, bright blood was noted in the gastric aspirate and the hematocrit fell. Twenty units of intravenous Pitressin resulted in prompt clearing of the aspirate and stabilization of the hematocrit. The patient was placed on increasing doses of intramuscular Pitressin tannate with little effect. He experienced 5 additional episodes of major bleeding on the fourth, sixth, tenth, eleventh, and twelfth postoperative days. Each time the bleeding was rapidly controlled with intravenous Pitressin. Subsequent to the twelfth postoperative day the patient had no further bleeding, and he was discharged on April 3, 1957. (Fig. 3.)

In 2 patients, who were initially treated with an inflated Sengstaken-Blakemore tube which failed to control the bleeding, the addition of intravenously administered Pituitrin brought about a prompt cessation of bleeding (Table I).

On two occasions intravenous Pituitrin was used to facilitate transesophageal ligation of bleeding varices. Transthoracic esophagotomy resulted in brisk "arterial"-type bleeding which obscured the surgical field and made identification of the individual varices extremely difficult. Twenty units of surgical Pituitrin were administered over a period of 3 minutes with a dramatic reduction in the intensity of the bleeding, thus making the individual varices more apparent for suture.

A slight increase, approximately 20 mm. Hg, in brachial arterial pressure was occasionally noted either during administration or in the immediate post-injection period, but the pressure returned to normal after a maximum of 10 minutes. There were no significant alterations in nonprotein nitrogen, sodium, potassium, carbon dioxide, or chloride. Two of the patients treated with surgical Pituitrin for an acute bleeding episode complained of diffuse crampy abdominal pain, which subsided one-half hour subsequent to the completion of therapy.

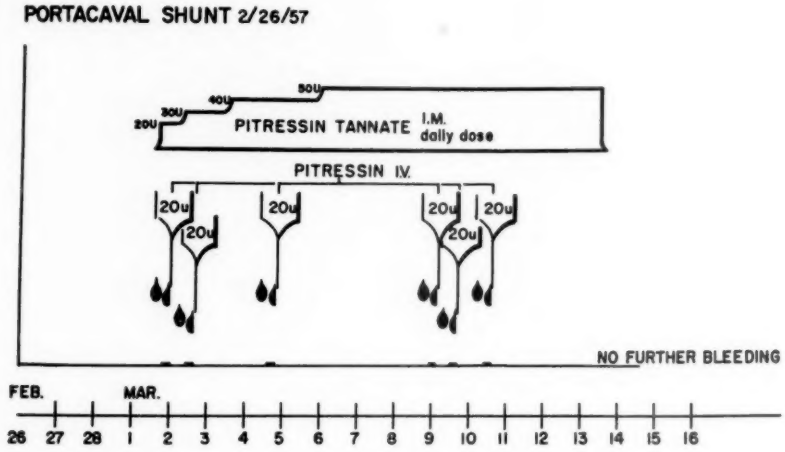
PORTACAVAL SHUNT 2/26/57
PITRESSIN TANNATE I.M. daily dose
PITRESSIN IV.
NO FURTHER BLEEDING
FEB.
MAR.
26 27 28 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16

Fig. 3.—Graphic representation of patient's hospital course indicating bleeding episodes and Pitressin control.

DISCUSSION

The management of acutely bleeding esophageal varices remains a difficult problem. In the patient with significant liver dysfunction, especially with jaundice, anesthesia and surgery frequently precipitate hepatic failure and coma. Nevertheless, immediate surgical attacks, either by transesophageal ligation[5, 9, 15] or portacaval anastomosis,[24] have been proposed in view of the unsuccessful results associated with the conservative regimen. Although the injection of bleeding esophageal varices with schlerosing solutions has enjoyed sporadic popularity,[8, 17, 20] the use of balloon tamponade has been the nonoperative method usually adopted for the control of esophageal hemorrhage. Several variations[1, 14, 22, 25, 29] of tamponade have been described since the initial report,[35] but the Sengstaken-Blakemore triple lumen tube[4, 30] is the most widely used. It has proved a great aid in the control of hemorrhage, but reports have indicated failure rates varying from 25 to 55 per cent[11, 16, 23, 27] and in our experience approximately 40 per cent of the bleeding episodes could not be controlled with tamponade. Aspiration, asphyxiation due to regurgitation of the inflated esophageal balloon with consequent obstruction of the airway, and ulceration at the site of tamponade have all been reported[3, 11, 34] and experienced in a significant number of instances in our clinic. An appreciable number of patients have complained of marked discomfort associated with esophageal tamponade and, since sedation is to be avoided with hepatic insufficiency, the problem is greatly intensified.

The lack of complete satisfaction with the tamponade approach and the desire to avoid extensive surgery in a patient with hepatic insufficiency prompted clinical investigation of a method which would intrinsically lower portal venous pressure. Intravenous surgical Pituitrin or Pitressin rapidly decreases portal hypertension and reduces bleeding from esophageal varices with consistent effectiveness. Subsequent to reduction of portal pressure the turgid veins collapse, as evidenced by esophagoscopy and direct inspection during esophagotomy for transesophageal ligation. The edges of the bleeding site can coapt, an hemostatic thrombus can form, and the patient may be tided over for a period, during which he is prepared for definitive surgery with a regimen directed at restoring liver compensation.

Esophagitis and ulceration play an important role in the development of bleeding from varices. Several investigators[2, 6, 33] have considered erosion of the mucosa the prime factor in the initiation of the bleeding episode. Supporting this concept is the occurrence of bleeding in the absence of portal hypertension.[19, 21, 26] It is therefore important to avoid further irritation of the esophageal mucosa by balloon tamponade. For this reason, a trial of the Pituitrin regimen should be carried out before resorting to technical pressure on varices. Also in consideration of the esophagitis factor, intravenous Pituitrin should be accompanied by constant nasogastric tube or gastrostomy drainage to prevent regurgitation of gastric acid in addition to determining the status of bleeding.

Twenty clinical units of surgical Pituitrin or Pitressin are diluted in 200 c.c. of 5 per cent dextrose in distilled water and administered intravenously over a 20 to 30-minute period when the diagnosis of acutely bleeding esophageal varices is made. Rapid infusion is necessitated by the tachyphylactic property of the drug. Therapy can be repeated at 4-hour intervals if there is evidence of continued or recurrent bleeding. Our two experiences with long-acting intramuscular pitressin tannate, coupled with the results in the treatment of hemoptysis,[32] suggest that Pituitrin and Pitressin are ineffective when administered intramuscularly and that rapid intravenous infusion is necessary. Arterial pressure is checked at 5-minute intervals during administration and the rate of infusion is slowed if marked elevation of blood pressure occurs. No specific treatment is necessary for abdominal cramps since they are transitory and will disappear when drug therapy is completed. Pituitrin and Pitressin are theoretically contraindicated in a patient witih a past history of coronary thrombosis or angina pectoris because both drugs are coronary vasoconstrictors. On one occasion 20 units of surgical Pituitrin were given to a patient whose electrocardiogram, taken at a later date, demonstrated an old posterior myocardial infarct. There were no untoward effects.

SUMMARY

Surgical Pituitrin and Pitressin are worth-while additions to the therapy of bleeding varices. Direct portal venous pressure measurements in patients with esophageal varices have demonstrated that intravenously administered surgical Pituitrin results in a rapid and marked decrease in portal pressure, equivalent to the level achieved by portacaval shunt. The drugs have proved effective

in the control of acutely bleeding esophageal varices and have been helpful in facilitating transesophageal ligation of bleeding varices. It is recommended that an intravenous surgical Pituitrin or Pitressin regimen be given an initial trial in the control of bleeding in view of the distinct advantages over balloon tamponade.

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DISCUSSION

DR. ROBERT R. LINTON (Brookline, Mass.).—The method almost sounds too simple, but one must admit the results are excellent. I would be a little fearful that the thrombus which forms to occlude the bleeding varix might dissolve and bleeding would recommence before one had sufficient time to prepare the patient for a shunt procedure. There is no question but that the acute bleeder presents a tremendous problem in most centers. It has always seemed to me that the best method of controlling a bleeding blood vessel is to ligate it. This certainly is true in the case of a lacerated or divided artery. It is my opinion that transthoracic esophageal suture of bleeding esophageal varices has not been generally accepted, because of indecision and procrastination. I believe a true surgical emergency exists when a balloon tamponade of the cardioesophageal junction is necessary to control the bleeding. Too often when tamponage is used alone bleeding may recommence a day or two after the balloon tube is removed and then finally the esophageal varices are sutured after the patient has been starved for 3 or 4 days, which is, in my opinion, poor surgical preparation for patients with sick livers such as most of these cases exhibit. As a result of these distressing results with the nonsurgical treatment it has been my rule for the past 7 years that, if balloon tamponade is necessary to control esophageal bleeding, an emergency suture of the varices should be performed, unless the patient is markedly jaundiced or in a comatosed state.

The surgical mortality in my own hands for the transthoracic esophageal suture of bleeding esophageal varices is around 20 per cent. This is higher than one would like, but lower, I think, than most other methods that have been utilized. I think what Dr. Mahoney and his co-workers have presented today may be an additional adjunct in the emergency treatment of bleeding esophageal varices and is worthy of further trial.

I am not sure that I have understood everything that has been presented in regard to the length of time that the portal pressure is reduced following the administration of the Pituitrin. The slides only show the venous pressure for a matter of 12 minutes which hardly seems long enough to be effective as a treatment in itself, and perhaps this point could be further discussed. Another point I would like to raise is, what was your mortality rate and were there any untoward effects of this method of treatment?

DR. BEN EISEMAN (Denver, Colo.).—My associate, Dr. William Silen, and I have been particularly interested in the possible role that arteriovenous shunts within the portal system may play in producing portal hypertension and have studied the action of various drugs and types of nerve stimulation in this regard in the experimental animal. We have

utilized a splenectomized Eck-fistula dog, which avoids any intrahepatic mechanism altering the portal pressure. The mechanism by which Pitressin lowers portal pressure as noted by Drs. Schwartz and Mahoney today, may be by closing such arteriovenous shunts—an action that is in keeping with the other known pharmacologic properties of this drug.

DR. FRANK GERBODE (San Francisco, Calif.).—I'd like to ask whether or not he believes the arteriovenous shunts which some people have described in the gastric circulation might have some effect on what he has seen.

DR. SCHWARTZ (closing).—In response to Dr. Linton's points, studies performed by Dr. Davis in Boston indicated that not only did Pituitrin decrease portal tension but that portal flow was also decreased. There was no mortality or increased morbidity which could be associated with Pituitrin administration. The point that Dr. Linton raises about the time is a very excellent one. Our slides only indicate a study for 15 minutes, they do not indicate how long the action of the drug persists. Studies done in dogs have indicated a time varying between 45 and 60 minutes, and we do propose in the future to cannulate some of the obvious veins on the abdominal wall and determine the exact length of time that these drugs will act.

As far as the questions raised by Dr. Eiseman and Dr. Shumacker, the course of action of the drug, they have hit on one of the two camps and two theories as to the action; namely, closing of arteriovenous shunts. More people, however, feel that the action is a direct action, constricting the splanchnic arterioles. After Pituitrin or Pitressin is administered, there is an actual decrease in the size of the liver as has been measured by Dr. McMichael and others from England.

EXPERIMENTAL PRODUCTION OF DISSECTING ANEURYSMS OF THE AORTA

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NOW that dissecting aortic aneurysms are amenable to surgical therapy, information regarding etiology and course of the disease has become extremely important.

The diversity of opinions concerning the etiology of dissecting aneurysms stands as open evidence of our lack of real knowledge of this aspect of the problem. Indeed, it is doubtful that there can be a single factor or chain of events consistently producing the changes leading to dissection of the aortic wall. From a review of the reported cases, it must be assumed that with rare exceptions (acute trauma and so forth), medial disease of varying nature is the basic and preliminary occurrence. In general, medial degeneration falls into two major categories—the primarily elastic degeneration seen in young patients (under 40) and the smooth muscle degeneration in older patients.[6] As a result of medial disease, the vasa vasorum are inadequately supported and rupture with the formation of a medial hematoma which separates the layers of the aortic wall. This eventually ruptures through the intima admitting blood under arterial pressure into the hematoma and extending the dissection perhaps even into normal tissue.

The course of the disease was classified into three major types by Gager[4] in 1929: (1) rupture of the intima, dissection of the media, and perforation of the adventitia occurring in a few seconds or minutes and causing death; (2) a slower process involving intimal tear and collapse of the patient, followed by freedom from pain for varying periods but terminating in more pain, rupture, and death; and (3) rupture of the sac into the lumen of the aorta with long survival or, very rarely, healing.

Length of survival after the onset of dissecting aneurysm is of major importance in surgical therapy and authorities differ widely in their reports of this. Mote,[13] quoting from the San Francisco coroner's office, stated that 30 per cent were found dead, 65 per cent were dead in 24 hours, and 96.7 per cent were dead in one month. Osgood[14] found 65 per cent dead in a few

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minutes and Sailer[16] noted 80 per cent dead in 48 hours (17 per cent suddenly) and 65 per cent of Shennan's patients[21] had expired in 24 hours. Contrastingly, Levinson[12] found only 36 per cent dead in 48 hours and only 58 per cent in 10 days. These data indicate that probably more than half of the patients with dissecting aneurysms will die in 48 hours and only 10 per cent or less will rupture into the aortic lumen and survive for any length of time.

When "healing" occurs by intraluminal rupture, this rupture is generally located at the distal end of the sac and the site is determined by weaknesses of the inner wall, by atherosclerotic plaques, or by vascular branches encountered by the progressing sac.[8] Jones and Langley[10] noted that 72 per cent of patients whose sacs recommunicate in this fashion survive more than 5 weeks, while only 4 per cent without recommunication survive that long. In the opinion of Weiss,[23] this newly-formed "double aorta" can function for years giving the patient a symptom-free existence and a normal work capacity. Endothelium rapidly forms in the new channel, but, unfortunately, this tends more strongly to atheromatosis than does that of the normal lumen.

Certain statistical points figure heavily in the choice of a surgical procedure for management of dissecting aneurysms. Fifty-five to 75 per cent originate in the ascending aorta.[13] Thirty per cent are confined to the ascending aorta.[21] Forty-seven per cent never dissect beyond the left subclavian artery.[21] Only 35 to 40 per cent even reach the abdominal aorta.[21] Ninety-five per cent of dissecting aneurysms which terminate fatally in the acute phase do so from external rupture.[1, 11, 21] Seventy per cent of all cases rupture into the pericardium and death results from cardiac tamponade.[1, 14, 21] Ninety per cent of those in which the intrapericardial aorta is involved terminate in this fashion.[21] "Healing" takes place by rupture of the distal end of the sac into the true lumen of the aorta.[20, 21] Only 5 per cent who "heal" die from later extension of the same dissection. Five per cent die from a new dissection and 10 per cent from saccular aneurysm secondary to the dissecting aneurysm.[21]

The study of dissecting aneurysms in an attempt further to understand their behavior has been complicated by the difficulty in consistently producing them in experimental animals. The condition has been produced in rabbits, hamsters, and guinea pigs by repeated injections of epinephrine, cortisone, and diphtheria toxin,[3, 22] but these animals died promptly if dissection developed and were too small for careful evaluation. Several investigators found that the pressure required to separate the layers of the media in the excised normal aorta was so high they concluded dissection could not be produced without aortic disease.[15] Dogs, possibly because of excellent blood supply to the aortic wall, are highly resistant to medial necrosis.[17, 18] Arteriosclerosis, when produced in these animals, generally damages only the subintimal tissues.

In spite of previously recorded failures with this technique,[5] we believed that if a pocket could be mechanically dissected within the media of the dog's aorta and aortic blood under normal pressure allowed to enter this pocket, a dissecting aneurysm would result. This was attempted in the manner illustrated in 26 animals. These were selected at random and were dogs of all ages with presumably normal aortas.

METHODS

Large dogs (approximately 18 Kg.) were selected and anesthetized with intravenous Nembutal. After insertion of an endotracheal tube, thoracotomy was accomplished through the left fourth intercostal space. The descending arch of the aorta was mobilized and the highest two intercostal arteries ligated. A vascular clamp was placed across the aorta proximally as shown in Fig. 1, and a short transverse incision made into the media. A plane of cleavage was developed between the laminae of the media 1 cm. proximally, 2 to 3 cm. distally, and extending approximately half the circumference of the aorta. We found it quite difficult to stay at the same level within the media. After occluding the aorta distally, a small ellipse of the inner wall of the pocket was excised to communicate the cavity with the aortic lumen. To insure free entrance of blood, the inner lip of the sac was sutured laterally to the aortic wall stabilizing the opening in a funnel-like position. The initial incision through adventitia and outer media was then closed and the occluding clamps released. This procedure was repeated in 25 similar dogs. The plane of cleavage was opened 2 to 3 cm. in a proximal direction in four of these animals.

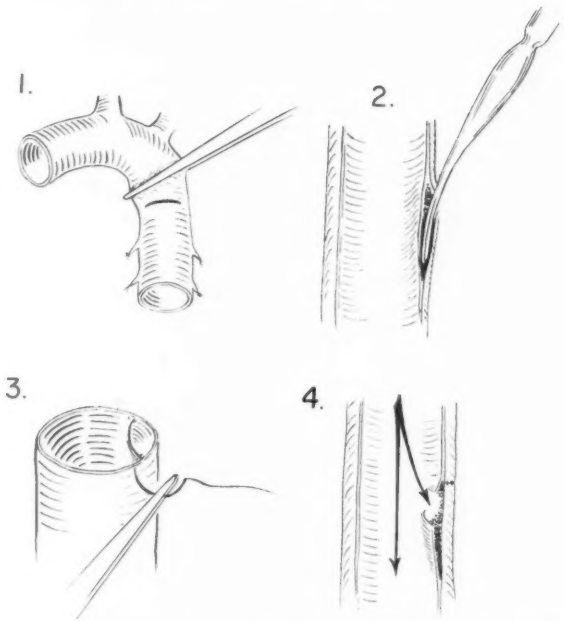

Fig. 1.—(*1*) Position of the proximal aortic clamp and location of the initial incision into the media. (*2*) Development of the plane between the laminae of the media. (*3*) Suture of the inner lip of the sac to the lateral wall of the aorta. (*4*) Procedure completed. The ellipse of intima has been excised and the original incision closed.

In 4 animals, a narrow dissection was made 2 to 3 cm. in length, a large bore Tygon cannula inserted, and the neck of this sac tightened around the cannula using a 3-0 silk suture. Saline was injected through this cannula in an attempt to separate the layers of the media by hydrostatic pressure. This was performed in a proximal direction in two dogs and in a distal direction in two.

In an attempt to simulate the effect of hypertension on this process, Levophed was administered intravenously to 3 dogs after the aortotomy was closed.

Initially, pressures were taken through a No. 18-gauge needle proximal to the sac, within the sac, and distal to it immediately upon release of the occluding clamps. One week following dissection, pressures were determined proximal and distal to the sac by cannulae inserted into the aorta through the brachial and femoral arteries.

A pressure cannula was placed in the sac in 5 animals and placed in various positions during the dissection. A simultaneous pressure was recorded at the aortic bifurcation, and the pressure recorded by the proximal cannula at the mouth of the sac was accepted as equal to that within the aortic arch.

One animal was allowed to live 7 months following operation, and at sacrifice was noted to have developed slight aneurysmal dilatation at the site of excision of the segment of internal wall. Three other dogs were kept alive for 5 months to further evaluate this finding.

All of the aortas were preserved in formalin, and histologic studies with hematoxylin and eosin and Verhoeff's elastic stains were carried out.

RESULTS

Blood distended the mechanically created sacs after release of the occluding clamps and continued separating the layers of the media producing a dissecting aneurysm. Extension of the initial sac to more than four times its original length occurred in 13 of the 26 dogs in which dissection was initiated in this fashion. Twelve dogs failed to develop dissection because of internal rupture of the sac during preparation or because of hypotension from hemorrhage through the aortic incision.

Six of the 13 dissecting aneurysms remained blind and thrombosed after extension while 7 ruptured into the lumen at the depths of the dissection and remained patent. The thrombosed sacs projected into the lumen of the aorta and at the time of autopsy appeared sufficiently distended to constrict the lumen markedly. In no cases did proximal extension occur even though the aorta was occluded distal to the intimal opening in an attempt to facilitate dissection in this direction.

In one animal the mechanically produced sac extended 3 or 4 cm. and ruptured into the retropleural tissues creating a large hematoma. This was the only incidence of external rupture.

No extension was noted in the two animals in which we produced initial sacs directed proximally by injection of saline even though the sacs extended around the branches of the aortic arch. These injections resulted in sacs whose only openings were at the distal extremity. They remained collapsed and, in one, early healing was noted at autopsy. Injection distally produced one sac which extended to the celiac artery upon admission of blood, distended, and clotted. The other ruptured into the lumen during injection.

Administration of vasopressors produced a dramatic increase in the rapidity and violence of the dissecting process. In all 3 animals the time required for dissection through the thoracic aorta was shortened from 2 or 3 minutes to 4 or 5 seconds.

The needle pressures which were taken in the initial 5 animals showed essentially identical values above, within, and below the sac. Proximal and distal pressures measured in 5 animals one week postoperatively also showed no significant gradient, even though autopsy revealed two of them to have clotted sacs impinging on the aortic lumen. When the pressure cannula was passed up and down within the sac during dissection, we noted that in all 5 animals the pressures at all levels within the sac were identical to that in the proximal aorta except at the distal tip where we believed that apposition of the walls of the sac caused damping of the pressure tracing. In 2 animals immediately after release of the clamps, the bifurcation cannula recorded a

low pressure with almost no pulsation. The sac was markedly distended and the pressure within it was normal with a normal aortic pulse. At the moment decompression through the intima was observed, the pressure and amplitude of the pulse wave at the bifurcation became almost identical to that within the sac (Fig. 2). We felt that this mechanism explains the phenomenon of absent and reappearing pulses occurring frequently in human dissecting aneurysms.

Only 2 of the 4 dogs selected to evaluate aneurysm formation at the site of intimal defect developed any appreciable dilatation (Fig. 3). The dilatation in the second was not so marked as that in the one which initiated the study.

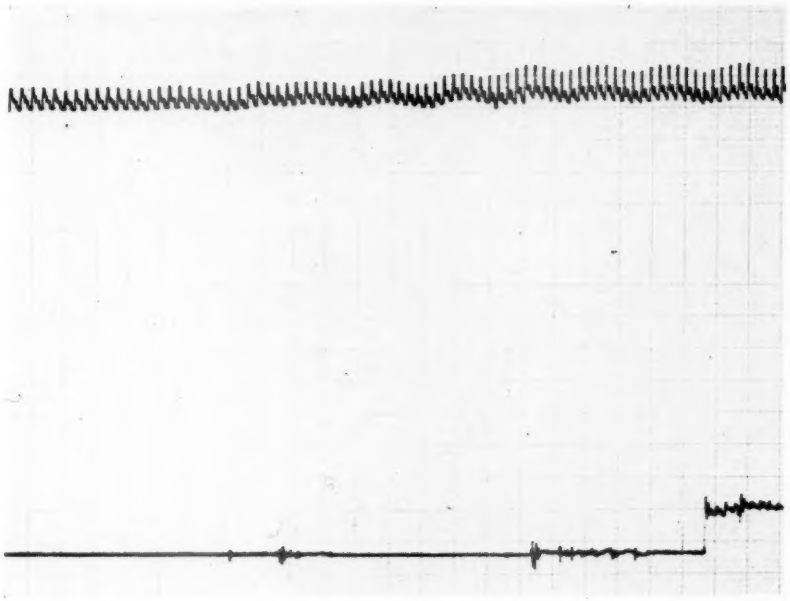

Fig. 2.—Tracings showing pressures within and below a dissecting sac. The upper tracing represents the pressure within the sac while the lower shows the low pressure and absence of pulses at the bifurcation during the progress of dissection. Rupture into the lumen with decompression of the sac is seen at the lower right where the bifurcation pressure increases abruptly.

On histologic examination these dissections ranged from approximately halfway through the media to the junction of the medial and inner thirds. Thus they differ from human dissections in that the latter are most usually located at the junction of medial and outer thirds. New endothelium rapidly formed within the recommunicating sacs and in one short dissection this was present although the animal died only 5 days following operation.

In both clotted sacs and long recommunicating ones, a wedge of scar tissue involving muscle and elastica was noted at the tip of the dissection on longitudinal section and in the lateral clefts on transverse section. In the recommunicating sacs fibrous tissue seemed to thicken both internal and external walls, and there was a marked tendency to form new elastic fibrils within this scar. This phenomenon appears to represent necrosis of elastica with regeneration rather than formation of a new wall within scar or organized clot, because smooth muscle cells were present in the same area and these do not regenerate.

A constant finding along inner and outer walls of the sacs was destruction of smooth muscle. Adjacent to the sac was seen a layer of smooth muscle necrosis made up entirely of cells from which the nuclei had disappeared. Next to this was a layer of cellular edema surrounded by histologically normal smooth muscle.

DISCUSSION

This experiment shows that dissecting aneurysms of considerable length can be produced in the presumably normal dog by admitting blood under normal arterial pressure through an intimal rent into a sac previously prepared within the substance of the media. Dissections extended to the diaphragm in all our cases, to the celiac artery in most, and to the renal artery in one animal. Extension occurred in all cases provided the original sac was blind, was greater than 1 cm. in length, and provided that the dog was not hypotensive at the time blood was admitted to the sac. In no animals did any proximal dissection occur even when a proximal pocket was prepared equal in size to the distal one. The site of spontaneous rupture through the intima after extension was determined in almost all cases by the location of large branches. The distal intimal tears were generally found at the ostium of the celiac artery.

Fig. 3.—Short sac with aneurysmal dilatation at the site of intimal defect. The internal surface of the aneurysm is seen through the defect.

It was apparent also that the aortas of some of the dogs were more resistant to dissection than others, and this was entirely irrespective of age or general physical condition. This was evidenced by difficulty in separating medial lamellae with the dissector and also by the fact that several dissections stopped at the diaphragm, distended with blood, and clotted. This cessation of dissection was felt to be due to dissipation of pressure at the depths of the

sac because of peripheral resistance along its course. The slightly lowered pressure was inadequate to separate the layers in the aortas with above average lamellar cohesive strength.

If the distal perforation was tiny, it frequently thrombosed and the sac filled again with blood which later organized. Numerous intercostal arteries were sheared off by the progress of most of the dissections and although each provided an open recommunication with the lumen, they did not decompress the sac sufficiently to prevent extension throughout the entire thoracic aorta (Figs. 5-7).

The applicability to human cases of such data determined in the dog is somewhat uncertain. It is well known that the dog is far more resistant to medial necrosis and atherosclerosis than is the human, and Schlichter[18] attributed this to the more adequate vascular supply to the vessel wall. It is also well known that the dog's aorta may be more friable and difficult to suture than is the human vessel. However, the pressure required to rupture the dog's aorta is of similar magnitude to that required to rupture the human aorta.

This work seems to indicate that even in the human, hypertension is not a necessary factor but, when present, the dissecting process is much more rapid and violent. It also seems probable that in humans once a dissection begins, it may extend into normal aorta, particularly in the presence of elevated blood pressure.

Our observations substantiate the theories of Hoff[7] concerning disappearance and reappearance of peripheral pulses. He reasoned that a distended sac could block blood flow and decompression would permit its passage again.

In our animals, the site of rupture was determined by an obstruction to the progress of dissection such as is produced by major branches of the aorta. We observed in the sacs no pressure changes which could contribute to rupture.

Inability to produce a proximally directed dissection by this technique suggests that in humans, simple admission of blood from the lumen into a space between the layers of the aortic media would not result in a dissecting aneurysm extending proximally. This tends to substantiate the theory that dissecting aneurysm is preceded by medial hematoma without a break in the intima. It suggests that the proximal extent of the dissection is determined by the extent of the hematoma and that the subsequent intimal tear does not cause any proximal dissection. We believe that the intimal tear is secondary with regard to involvement of the proximal aorta, but its occurrence promotes extension of the sac in a distal direction. Hypertension exerts a significant effect on the extent and rapidity of the distal progress. Because of these results, we feel that the DeBakey procedure[2] is effective therapy even in the rare cases in which no intimal defect is present. The creation of an intimal defect would not cause proximal progression. The distal portion of the sac is closed in this procedure and does not communicate with the defect.

Aneurysmal dilatation of the external wall of the sac opposite defects in the internal wall attests to the value of wrapping such areas with Orlon fabric. Such support seems indicated at the area of surgical decompression as well as in the ascending aorta where intimal tears frequently are found and terminal rupture most often occurs.

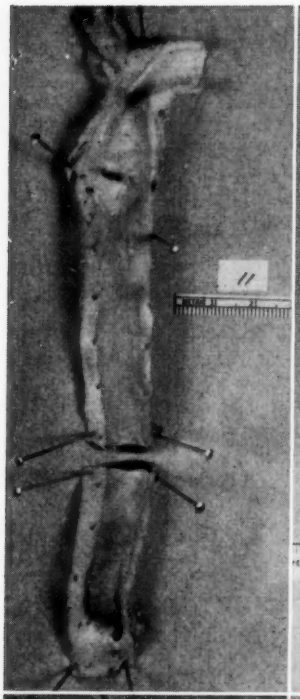

Fig. 4.

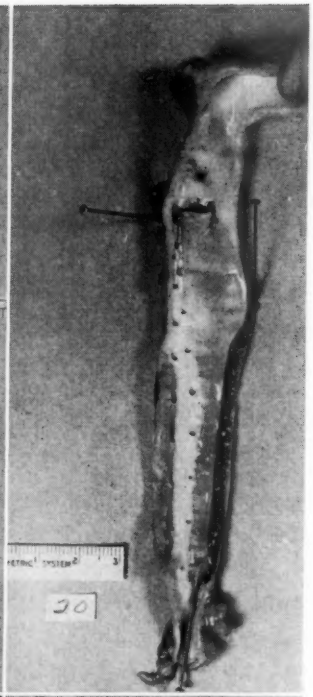

Fig. 5.

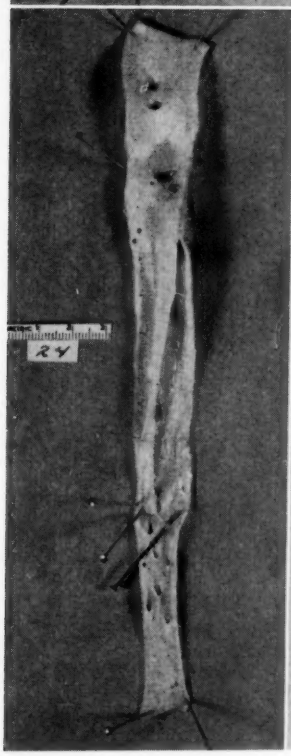

Fig. 6.

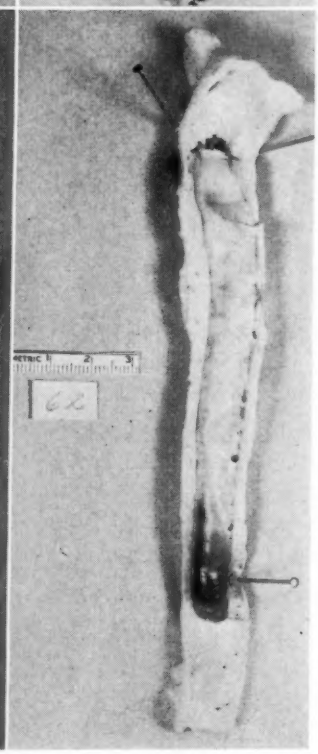

Fig. 7.

Fig. 4.—A preserved specimen showing a dissection which extended to the ostium of the celiac artery and clotted. The specimen has been cut to show a cross section of the sac.

Fig. 5.—Dissecting aneurysm extending almost to the celiac artery with rupture into the lumen. The lower pin lies in the rupture. The sac is open and filled with soft clot. The intercostal arteries at the left communicate with the sac.

Fig. 6.—This aneurysm ruptured into the lumen at the level of the celiac artery. Rupture site is marked with a pin. Intercostal arteries communicate with this sac and the sac is lined with endothelium.

Fig. 7.—Thrombosed sac extending to the region just above the celiac artery. Intercostal vessels communicate with it.

Our sacs created proximally from an intimal defect neither extended nor even distended with blood. This suggests closure of the so-called initial intimal tear with decompression of the distal extremity of the sac as an effective form of surgical therapy and one providing drainage of the entire extent of medial hematoma. This situation in the animal resulted in collapse of the sac with early healing across the medial cleft. Unfortunately, the tendency toward rigid sclerosis in humans with this disease might prevent a complete "cure" from a similar decompression and only one case of such healing has been recorded. However, since the medial hematoma results from bleeding vasa vasorum prior to an intimal tear, the DeBakey procedure of decompression of the proximal part of the sac in the thoracic aorta with closure of the distal part of the sac converts this distal sac into a closed medial hematoma. Further bleeding from the vasa vasorum could cause further distal extension of the sac and perhaps sufficient distention to compromise blood flow through the large abdominal branches. Shaw's[19] and Johns'[9] cases died in renal failure after operation, perhaps due to this phenomenon. Decompression of the sac at its distal extremity might prevent this.

Dissecting aneurysms produced in this manner do not result in the same clinical course as do spontaneous dissections in human patients. In only one of our 30 animals did external rupture occur, and the aortic walls were not sclerotic as is seen so frequently in humans. However, this preparation in dogs has raised several points which seem to merit further thought and investigation.

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Discussion

DR. ALEXANDER BLAIN (Detroit, Mich.).—One thing should be stressed and has been mentioned by Dr. Blanton, although it has not been stressed in the experimental approach to producing this lesion. This is the fact that dissecting aneurysms can occur without an intimal rupture. Most textbooks on pathology have traditionally stated that intimal rupture is the primary event in the pathogenesis of this lesion. Possibly the first known case occurring without intimal tear was reported in the nineteenth century by Krukenberg in Germany and this was a dissection of a subclavian artery which was an incidental finding at autopsy.

Now that surgical progress has recently been made in the treatment of this lesion by Gerbasi, and by Cooley and DeBakey, it is important for further steps in surgical technique to be developed. These steps will be facilitated by the realization that while intimal tears are seen in most of these lesions, the lesion can occur without an intimal tear and, therefore, presumably the hematoma is the primary and sometimes the only lesion.

DR. DEAN K. CRYSTAL (Seattle, Wash.).—I, too, have endeavored to reproduce this lesion in a laboratory and have failed. A colleague of mine in physiology has told me that a dissecting aneurysm actually is an impossibility. There is nothing about the theoretical dynamics in the aorta which permits a dissecting aneurysm to develop.

On that basis we have come to the hypothesis that the way a dissecting aneurysm may come about is as follows: We think that with each systole there is an elongation of the aorta with a recoil. Each snap-back allows one coat of the aorta to work on another, as it were, within the wall. A primary weakness within the aortic wall will allow the movement of one layer of the wall on the other to become more and more marked.

We cannot prove this, but we wonder whether the so-called primary dissection in the opening between the main aortic lumen and the hematoma which forms at the site of weakness may not in some instances actually be secondary, as Doctor Blain said a moment ago.

DR. BLANTON (closing).—I appreciate Dr. Blain's discussion very much because I have read all the articles I think that he has written on the subject and some of them were very stimulating to this particular work.

AN ANALYSIS OF THE PATHOLOGIC ANATOMY OF PULMONARY ARTERIOVENOUS ANEURYSMS WITH PARTICULAR REFERENCE TO THE APPLICABILITY OF LOCAL EXCISION

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WE HAVE undertaken an analysis of the gross pathologic anatomy of pulmonary arteriovenous aneurysms in an effort to clarify the applicability of local excision and also to gain some insight into the likelihood of incomplete excision or recurrence as a result of a limited resection. Two hundred and fifty-two published cases from the world literature have been studied and to these have been added 98 previously unpublished cases submitted to us on a questionnaire, a total of 350 cases. We have exercised great care to avoid including a case more than once in our statistics. Many pertinent data are missing from some of the descriptions. A very limited number of autopsy cases is available in which complete study of the lungs has been carried out by injection techniques.

In many instances the pulmonary lesions represent manifestations of a more generalized disease, hereditary telangiectasia or Osler-Weber-Rendu disease. This relationship with Osler-Weber-Rendu disease was present in 36 per cent of patients with single arteriovenous aneurysms and in 57 per cent of patients with multiple arteriovenous aneurysms. A positive relationship was accepted on a basis of a familial history, significant epistaxis or bleeding from other organs, or the presence of other telangiectasia, either cutaneous or visceral.

The wide variability of the pulmonary manifestations is impressive. No one pathologic term satisfactorily describes the lesions in all cases. Pulmonary telangiectasia, arteriovenous fistula, arteriovenous aneurysm, and arteriovenous varix are terms, each of which in an individual case may seem most descriptive. On the one extreme, there are the multiple pulmonary telangiectasia, minute arteriovenous fistulas which are distributed through all lobes of both lungs. On the other extreme there is the single large arteriovenous aneurysm which produces marked clinical manifestations. In between there is a wide range of cases with minute, small, or large fistulas, scattered or localized, in some instances producing little difficulty, in others, marked symptoms. The configuration of the lesions varies considerably. The large size of the sac is often impressive, particularly when single, and the feeder vessels are usually limited to one or two large arteries and veins. The arteries tend to be thin-walled and dilated;

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the veins may exhibit a wall thicker than normal. The wall of the sac may be thick in some areas, thin in others, and degenerative changes including calcium deposition are not infrequently observed. In other instances, however, convoluted masses of dilated thin-walled vessels with multiple communications dominate the picture. In occasional instances an entire segment and even a lobe may be largely infiltrated and replaced by the pathologic process. Cases have been described in which a varix of thin-walled vessels spreads out over the surface of the lung like a Medusa head.

Cases of pulmonary telangiectasia with multiple, minute arteriovenous fistulas, diffusely distributed, have been infrequently recognized, and less frequently studied. Brink[6] was perhaps the first to suggest this condition as an explanation for cyanosis in a patient with hereditary telangiectasia in whom both the chest roentgenogram and the angiocardiogram were negative. A more aggressive approach to this obscure problem can be credited to Cooley and McNamara[11] who were able to confirm by lung biopsy the suspicion of pulmonary telangiectasia in a cyanotic patient in whom both the conventional film of the chest and the angiocardiogram were essentially negative. The authors did call attention to a curious beaded appearance of the small pulmonary arteries seen on the angiogram. Many tiny telangiectasia were observed on the surface of the lung and these lesions were also demonstrated by histologic study. Although the arteriovenous communications were too small to be visualized by roentgenographic techniques a sufficiently large right-to-left shunt was present to reduce the arterial oxygen saturation to 81.4 per cent. Sacrez[29] was able to demonstrate tiny arteriovenous fistulas by angiocardiography. Hales[18] found only 7 cases of this type in the literature. He added two cases which are beautifully documented by Vinylite injection-corrosion techniques. Both patients were cyanotic and in one the arterial oxygen saturation ranged between 70 and 80 per cent. Roentgenograms were negative in both—and the angiocardiogram in one—of the two patients. In the most carefully studied patient Hales demonstrated several hundred plexiform arteriovenous fistulas uniformly scattered through all lobes of both lungs. The plexuses varied from 1 to 10 mm. in diameter. The author concluded that the "lesions consisted of dense plexuses of tiny vessels connecting dilated pulmonary arteries and veins. Lesions intermediate in type between plexuses and saccular aneurysms indicate that the latter may arise by progressive dilatation of one of several limbs of the small plexuses."

Jones[8-33] records in our survey a cyanotic patient, 30 years of age, who also had cirrhosis of the liver. A postmortem injection study of the lungs disclosed many tiny arteriovenous fistulas in both lungs. The arterial oxygen saturation was 82 per cent. Antemortem roentgenographic studies including angiography had been negative.

An interesting variation of pulmonary arteriovenous aneurysm has been observed in a small number of cases in which part or all of the arterial blood supply is derived from a systemic source. Four such cases are recorded in the literature[7, 20, 22, 35] and 8 are added from our survey. In 9 of the 12 cases the

systemic artery probably originated from the aorta and joined the aneurysm either directly or after a tortuous course. In 2 of the 3 remaining cases the systemic vessel arose from an intercostal artery and in the third instance from the pericardiophrenic artery. In at least one of the cases the intercostal supply may have been acquired secondarily through pleural adherence. The presence of vascular adhesions believed to have been secondarily acquired has been noted in a limited number of other cases not included in this group of 12, and in several instances has posed a major threat to the safe conduct of the operation. In the cases recorded by Jones[S-33] and by Geary,[S-23] the systemic artery represented the only artery to the fistula, whereas in the other cases the systemic artery served as an additional vascular contribution to the pulmonary arteriovenous fistula.* The physiologic significance of the systemic-pulmonary arteriovenous fistula is that a left-to-right as well as a right-to-left shunt is present and the arterial desaturation is partially nullified. Of surgical importance is the increased hazard from hemorrhage during the operative procedure. In the case of the intercostal-systemic contribution, notching of the ribs may be observed and was found in a case reported by Raymond.[S-53] This latter condition should be distinguished from an arteriovenous fistula confined entirely to the thoracic parietes, a condition well described by Maier.[24]

Tables I through IV summarize the anatomic disposition of pulmonary arteriovenous aneurysms in 350 cases. Sixty-four per cent of the specified cases were thought to represent single lesions. The higher percentage of patients with single lesions occurring in the recent survey group reflects the detection of relatively asymptomatic and acyanotic patients through routine x-ray examination. The information was insufficient in 21 of the cases to allow proper classification. Table II reveals that there is a somewhat higher percentage of the single lesions to be found in the lower lobes.

TABLE I. NUMBER OF CASES

	SURVEY	PUBLISHED	TOTAL
Single arteriovenous aneurysm	67	145	212
Multiple arteriovenous aneurysms	31	86	117
Number not specified	0	21	21
Total cases	98	252	350

TABLE II. LOCATION OF SINGLE ARTERIOVENOUS ANEURYSMS

Left upper lobe	36
Left lower lobe	56
Right upper lobe	17
Right middle lobe	34
Right lower lobe	50
Not specified	19
Total	212

In Table III the cases are listed according to the number of lesions reported per case. Sixty-eight are categorized as "multiple" or "not specified" because

*In a recent communication to us Dr. Harrison Black has added one more case of this type. Tortuous branches from the pericardiophrenic and internal mammary arteries joined a pulmonary arteriovenous aneurysm in the right middle lobe.

of a vague or indefinite description. The majority of this unspecified group, however, undoubtedly had more than three lesions. All cases with a diffuse form of the disease are listed with this group. In 30 cases of the entire group of 117, no more than two lesions were found.

TABLE III. MULTIPLE ARTERIOVENOUS ANEURYSMS

NUMBER OF ANEURYSMS	NUMBER OF CASES
2	30
3	7
4	7
5	2
6	1
7	2
"Multiple"	23
Not specified	45
Total	117

In Table IV the multiple lesions are grouped according to their regional location. Fifty are unilateral and 50 are bilateral, and 17 cases were not adequately specified. When the single arteriovenous aneurysms are grouped with the multiple unilateral cases, making a total of 262, it is apparent that approximately 75 per cent of the entire group may be considered unilateral. However, it is evident from the data in Table V on angiography that the figures presented in Table IV may be somewhat in error. Only 135 of the total 349 cases were subjected to this diagnostic study. In 20 cases arteriovenous fistulas or aneurysms were identified when these were not visible on the conventional plain film. It is probable that some of the so-called unilateral cases are in reality examples of bilateral arteriovenous fistulas which remained unproved because angiography was not employed. Furthermore, a number of cases have been reported in which previously undetected fistulas were encountered at operation. It is clear that the presence of a large arteriovenous aneurysm does not rule out the presence of other small, inconspicuous fistulas in the same or opposite lung.

TABLE IV. LOCATION OF MULTIPLE AVA

Unilateral		50	Bilateral		50
Same lobe		22	2 lobes	25	
Left upper lobe	5		3 lobes	15	
Left lower lobe	5		4 lobes	5	
Right upper lobe	2		5 lobes	5	
Right middle lobe	3				
Right lower lobe	7				
2 lobes		20			
3 lobes		8			
Not specified			17		

TABLE V. ANGIOGRAPHY

Confirmed x-ray findings	108
Located additional arteriovenous aneurysms	11
Diagnostic with negative x-ray	9
Failed to show arteriovenous aneurysms	7
Total	135

Since the first pneumonectomy performed for pulmonary arteriovenous aneurysm by Shenstone in 1940 and reported by Hepburn and Dauphineé in 1942,[19] there has been a trend toward conservatism in the surgical resection of these lesions. Janes[21] in 1941 and 1942 carried out bilateral local excisions. Whittaker[37] in 1944 resected a lobe for this disease but the patient died postoperatively. Blalock[32] apparently performed the first segmental resection for this disease. An increasing number of segmental resections was subsequently reported. It appears from our survey that local excision is being employed with increasing frequency. Twenty-one local excisions are among the total operative procedures listed in Table VI. Additional local and wedge resections are included in the 31 cases listed in the combination and miscellaneous grouping. Several arterial ligations are tabulated under "other."

TABLE VI. OPERATIVE PROCEDURES

Pneumonectomy	14
Lobectomy	125
Segmental resection	43
Wedge excision	4
Local excision	21
Other (includes combinations)	32
Total	239
Bilateral resections	19

A total of 239 patients has been operated upon out of the collected series of 350 cases with 13 operative deaths (Table VII). Nineteen of these patients had bilateral resections with 2 deaths. Three other patients had two separate procedures on the same lung with one death.

TABLE VII. RESULTS OF SURGICAL TREATMENT

	NUMBER OF PATIENTS
Cured	173
Improved	19
Unchanged	2
Operative death	13
No information	32
Total	239

Seventeen patients 10 years of age or younger have been operated upon for pulmonary arteriovenous aneurysm with only one death (Table VIII). Lobectomy was employed in all but one. Of interest is the fact that most of these patients had single lesions. All of the children were described as cyanotic. In the past some of these young patients have been diagnosed as having congenital heart disease of the cyanotic type. Fifty-two per cent of the entire series of 350 gave evidence of symptoms or signs prior to age 15, but only 13 per cent were hospitalized before the age of 15.

In some patients the disease tends to be slowly progressive, as judged not only by increasing disability and polycythemia, but by enlargement of the density seen on x-ray or by the appearance for the first time of a shadow in the lung fields. On the other hand some authors have stated that there

TABLE VIII

REPORTERS	AGE (YEARS)	RBC (MILLION)	LOCATION AND NUMBER OF AVA	OPERATIVE PROCEDURE	RESULT
Pinkham, 1958	½		LUL-1 LLL-M	LU lobectomy and wedge excision LLL	Cured
Schlosser and Harken, 1956	1½	6.67	LUL-1 LLL-1	?	Cured
Sweet, 1947	2		RML-1	Lobectomy	Cured
Husson, 1956	2½	5.9	RUL-1	Lobectomy	Cured
Mills, 1958	4		LLL-1	Lobectomy	Cured
Groves, 1958	4½	5.84	LLL-1	Lobectomy	Cured
Castellanas et al., 1950	5		RLL-1	Lobectomy	Cured
d'Allaines et al., 1950	5		LUL-1	Lobectomy	Cured
Middelbonere, 1952	6	7.34	RUL-1	Lobectomy	Cured
Garland & Anning, 1950	6	7.1	RML-1	Lobectomy	Cured
Santy et al., 1950	6		LUL-1	Lobectomy	Cured
Garland & Anning, 1950	7	5.2	LUL-1	Lobectomy and excision	Cured
Potts, 1958	7		RLL-1	Lobectomy	Cured
Mitchell, 1954	7½	5.33	LLL-1	Lobectomy	Cured
Friedlich et al., 1950	8		RML-1 RUL-M RLL-M	RM Lobectomy	Imp.
Goetz, 1957	10		RLL-1	Lobectomy	Died
Boerema & Brilmore, 1948	10	6.0	RUL RML	RU-RM Lobectomy	Cured

was no visible increase in the x-ray density over a period of some years. Large sacs have been described in infants. There is some evidence to suggest that removal of arteriovenous fistulas may stimulate development of other small and perhaps previously undetected lesions. Evidence for rapid progression or enlargement of residual lesions postoperatively has been presented by Adams and associates,[1, 10] by Baer and co-workers,[2] Parker and Stallworth,[27] and Ronald.[28] In 3 of the 4 cases, secondary operations were carried out because of persistence or exacerbation of symptoms in the presence of newly found lesions. It is logical perhaps to assume that not only would the excision of large arteriovenous fistulas but also the unnecessary sacrifice of normal pulmonary parenchyma tend to expand latent minute or small arteriovenous fistulas. The increased volume of blood flowing through the remaining pulmonary bed should tend to seek the areas of lowest resistance which are the arteriovenous fistulas. Further information on this important matter can only be had through late re-examination of surgically treated cases.

For these reasons it seems particularly important to conserve the maximum amount of functioning lung tissue. With this in mind we have sought information regarding the applicability of local excision, first carried out by Janes[21] in 1941. Data were collected which described the position of the lesions in relation to the visceral pleura (Table IX). In 110 cases of single arteriovenous aneurysms in which the information was available, 89 of these lesions were located either immediately subpleural or were only partially embedded in the parenchyma. We have assumed that in either of these two situations a local excision is often possible and especially when the bloodless technique is employed, whereas in the case of a deep aneurysm either segmental resection or lobectomy will be required. We have also rather arbitrarily assumed that where more than two large arteriovenous aneurysms are present in the same lobe local excision probably would not prove very practical. From the information available to us it appears that most surgeons attempting local excision of arteriovenous aneurysms have initially isolated the feeder arteries and veins. Crafoord[12] first called attention to the technique of isolating the blood supply to the lobe or lung in order to render the lung essentially bloodless and allow safe and rapid dissection of the local lesion. This technique was elaborated upon by Parker and Stallworth,[27] and we have utilized it in our own case reported in this article. The pulmonary artery and veins to the lung or lobe are first isolated and occluded. In order to obstruct the bronchial arterial circulation and avoid congestion of the isolated area, the bronchus is likewise isolated and occluded over a rubber tubing since this assures complete occlusion and minimizes damage to the bronchus. The aneurysmal sac is then incised and after observing the vascular orifices the sac is readily stripped away from the surrounding parenchyma while accomplishing individual ligation of the feeder vessels. We are acquainted only with the experimental studies of Blades and associates[4] on dogs regarding the safety of total pulmonary ischemia. These authors noted essentially no histologic changes in the lungs even after periods of occlusion lasting 360 minutes. In none of the experiments was there evidence of thrombosis, even though anticoagulants were not used. The same authors used survival after contralateral pneumonectomy as a yardstick to disclose alterations in function following varying periods of total pulmonary ischemia. They concluded that periods of occlusion longer than 30 minutes probably led to permanent alterations in pulmonary function. While we do not wish to challenge the general validity of the deduction, analysis of their experiments indicates that the survival figures probably are not statistically significant. It is evident that further information is needed to determine the safety and permissible period of total pulmonary ischemia and to learn whether intermittent alveolar ventilation with oxygen is desirable. Fortunately local excision can be performed rapidly in a bloodless field.

TABLE IX. DEPTH OF SINGLE ARTERIOVENOUS ANEURYSMS

Subpleural	46
Partially embedded	43
Deep	21
Not specified	104
Total	214

TABLE X. SYSTEMIC ARTERIAL OXYGEN

PER CENT SATURATION	NUMBER OF PATIENTS
46-55	1
56-65	7
66-75	24
76-85	23
86-90	26
91-95	14
96-100	6
Not specified	248
Total	349

In order to plan properly the surgical treatment of a patient with pulmonary arteriovenous aneurysm, a technically satisfactory angiogram should be executed preoperatively. The periphery of the lung fields must be included. Callahan and co-workers[8] showed the value of dye dilution curves in demonstrating the absence of right-to-left shunts in the contralateral lung, if the catheter can be properly positioned. Where the catheter can be inserted beyond the fistula on the involved side, additional information can be gained. This technique might well prove to be of value in the operating room in the localization of obscure fistulas. Eringa and associates[14] and Adams and co-workers[1] have demonstrated the usefulness of oximetry in the localization of deep fistulas and in evaluating the completeness of the operative excision. It is doubtful, however, that this method attains a high degree of accuracy.

It is apparent that one must individualize the surgical approach in each case. Local excision may be considered the preferred technique for superficially located aneurysms where a distinct sac is present. These anatomic criteria were present in at least 54 of the 98 survey cases. Where other small satellite aneurysms are associated with one large aneurysm or where a cirsoid arteriovenous varix is present, a more generous resection is undoubtedly needed. On the other hand, in a patient with one or two large aneurysms and with multiple telangiectatic lesions scattered throughout the remaining lung, it would seem most unwise to perform a pneumonectomy. The resection should be limited to the major disease. We feel that arterial ligation as an alternative to excision should be condemned because of the uncertainty of controlling the entire arterial supply to the fistula and because of the inevitable enhancement of the bronchial circulation if normal parenchyma is supplied by the ligated artery.

CASE REPORT

W. B. was admitted June 10, 1957, to the Medical College of Virginia Hospital. This 39-year-old white man had noted slightly cyanotic nails and lips together with some decrease in exercise tolerance for about 5 years. A mass had been noted in the left lung on chest roentgenogram in 1941 and he was consequently rejected from induction into the army. There was a history of epistaxis.

On physical examination blood pressure was 140/70. There was obvious mild cyanosis of the lips and nailbeds, with slight clubbing. There were telangiectatic spots on the lips, tongue, and face (Fig. 1). He stated that similar spots had been present on the face of his father and grandfather. There was a Grade II, low-pitched systolic murmur in the third and fourth intercostal spaces about 2 inches to the left of the sternum. No diastolic component was heard.

Laboratory data revealed a hemoglobin of 19.6 Gm., red blood cell count 6.6 million, hematocrit 55 per cent, and arterial oxygen saturation of 91 per cent at rest. Electrocardiogram was normal. Chest x-ray revealed a 7 by 6 cm. mass in the anterior left thorax with several adjacent smaller masses which in the lateral view tended to radiate from the hilum (Fig. 2). No significant enlargement apparently had occurred in the size

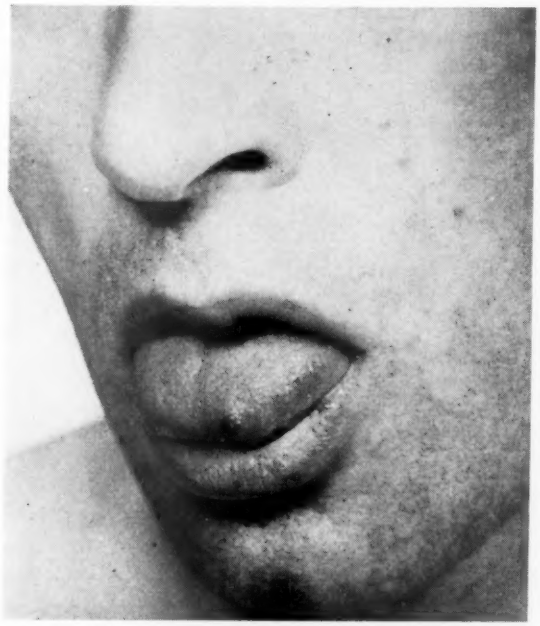

Fig. 1.—Note telangiectasia on cheek, lips, and tongue.

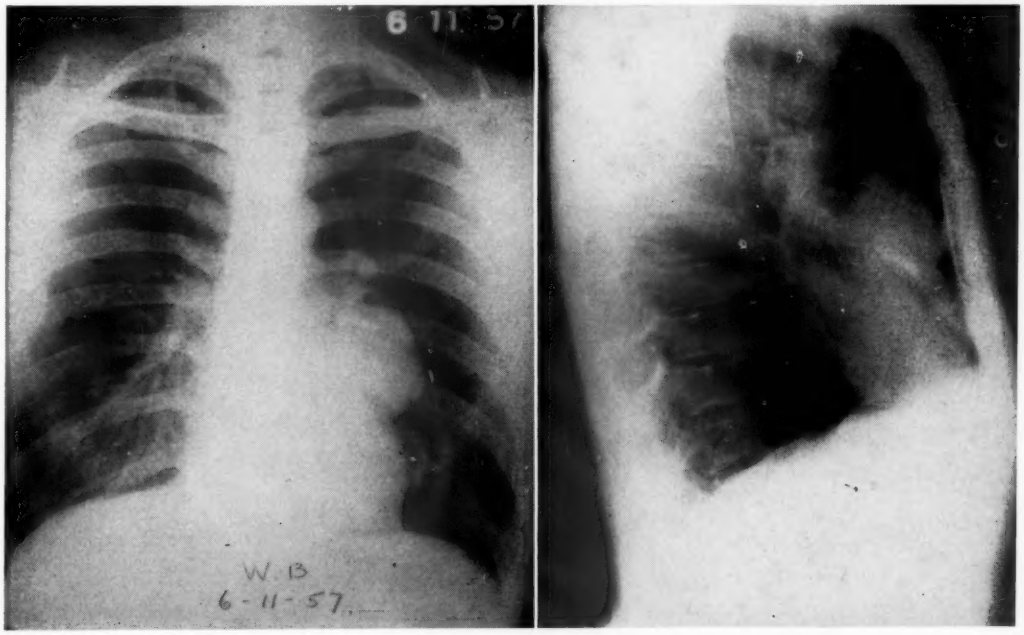

Fig. 2.—Posteroanterior and lateral chest films showing large aneurysm as well as adjacent vascular shadows.

of the mass over a period of 16 years as judged by the report from the previous chest film. On fluoroscopy the smaller densities showed fairly vigorous pulsation. There was intensification of the large mass on deep inspiration and blanching on forced expiration. Angiocardiogram was performed which showed early filling of the lesion with the contrast medium. The quality of the films was not sufficiently good for reproduction. No other pulmonary arteriovenous fistulas were noted.

Fig. 3.

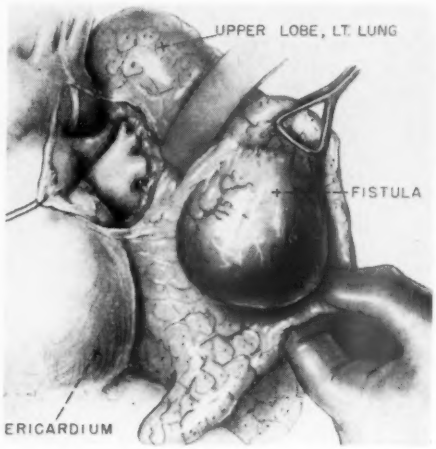

Fig. 4.

Fig. 3.—Thin-walled sac located immediately subpleural.
Fig. 4.—Large pulmonary arteriovenous aneurysm on the anterior segment.

Fig. 5.

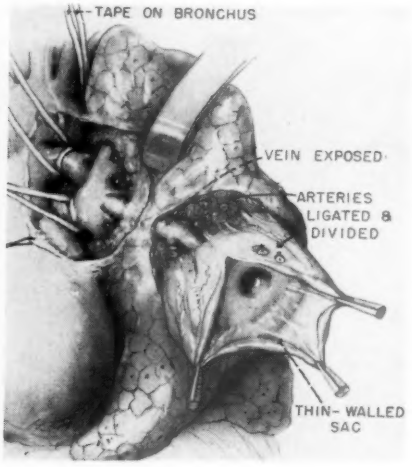

Fig. 6.

Fig. 5.—Opened sac under conditions of total pulmonary ischemia.
Fig. 6.—Opened sac in process of being stripped out. Not occlusion of hilar structures.

Operation was performed on June 17, 1957, and a large subpleural aneurysmal sac was found on the undersurface of the anterior segment of the left upper lobe (Figs. 3 and 4). The wall of the sac was very thin and there was a distinct thrill over the mass. After occlusion of the main pulmonary artery and superior pulmonary vein together with the main bronchus, the sac was entered and the vascular orifices were observed, two of

arterial origin 6 mm. in diameter each, and one of venous origin 1 cm. in diameter (Fig. 5). The two arteries were ligated individually close to the base of the sac but the large vein was dissected some distance proximally where it joined a vein from the anterior segment (Fig. 6). No other arteriovenous communications were noted.

The patient's postoperative course was uneventful. Re-examination one year later reveals that he has gained 20 pounds in weight. Previously noticed shortness of breath on exertion is no longer present. Arterial oxygen at rest and after exercise is 96 per cent. The hematocrit is 50 per cent and the red blood cell count is 5.98 million. Roentgenogram of the chest shows no areas suggesting arteriovenous aneurysms.

The pathologic examination of the sac revealed that the wall varied in thickness. "The thinner portions contain calcified plaques and are composed of a mixture of fibrous connective tissue, elastic tissue, and smooth muscle. This region has the appearance of a vein. An adjacent thicker portion more closely resembles an artery and the intima, media, and adventitia can be identified. Elastic tissue stains reveal a well-developed external elastic membrane but no clear-cut internal elastic membrane."

SUMMARY

1. Three hundred and fifty cases of pulmonary arteriovenous aneurysm (fistula), including 98 previously unpublished cases, have been reviewed.

2. The wide variability in the gross pathologic anatomy is emphasized ranging from multiple, diffuse, pulmonary telangiectasia to a single large aneurysm.

3. Twelve cases are recorded in which a systemic artery joined the aneurysm.

4. Approximately 64 per cent of the cases had single lesions and in 75 per cent the disease was unilateral.

5. Angiography should be performed preoperatively in all cases to detect fistulas which are not visualized on plain films of the chest.

6. Two hundred and thirty-nine cases have been treated surgically, in 19 of which bilateral resections were performed. There were 13 operative deaths.

7. Seventeen patients under the age of 10 have been operated upon, with good results in all but one.

8. A technique for performing local excision in a bloodless field is reemphasized and it is estimated that this can be employed in at least one-half of all cases, in preference to segmental resection or lobectomy.

9. A case report is presented which illustrates the applicability of this technique.

10. It is urged that surgeons report any cases of late recurrence which might elucidate further the problem of latent small pulmonary arteriovenous fistulas.

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Contributors

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The memberships of the American Association for Thoracic Surgery, the Southern Thoracic Surgical Association, and the Society for Vascular Surgery were canvassed for cases.

DISCUSSION

DR. F. HENRY ELLIS, JR. (Rochester, Minn.).—I merely would like to point out some of the hereditary aspects of this disease with which I am sure you are all familiar. A patient was recently operated upon at our institution who had multiple pulmonary arteriovenous fistulas. He came to the hospital accompanied by 5 brothers and sisters. Four of them proved also to have pulmonary arteriovenous fistulas. This prompted Dr.

Hodgson of our chest section to trace this family. He established a family tree consisting of 325 descendants of a German immigrant who came to this country some years ago. He secured information on two-thirds of them and found that 40 per cent had hereditary telangiectasia. He was also fortunate enough to be able to review the thoracic roentgenograms of 120 members of the group. Seven of them had pulmonary arteriovenous fistulas. An additional 6 in this same original group are known to have pulmonary arteriovenous fistulas, making a total of 13 out of this whole family group who have lesions of this type. It certainly behooves any of us who encounter patients of this sort to try our best to check into the family background and urge them all to have their chests x-rayed. Many of them may be harboring an unknown pulmonary arteriovenous fistula.

DR. FRANK GERBODE (San Francisco, Calif.).—We treated a young man who had a large pulmonary arteriovenous fistula with rather severe cyanosis. There was thrombocytopenia in association with it causing the wound to bleed quite a good deal postoperatively. After removing the pulmonary arteriovenous fistula by lobectomy, the thrombocytopenia and the coagulation deficit disappeared. We have wondered whether the old thought that the lung contributed something in platelet formation had something to do with this or whether it was only due to the chronic cyanosis. In any event, there was no question at all but that the thrombocytopenia was relieved when the fistula was removed. I would like to ask Dr. Bosher if in collecting these cases he had encountered this as a characteristic phenomenon.

DR. BOSHER (closing).—The thrombocytopenia which you observed is probably similar to that seen in some very cyanotic patients with tetralogy of Fallot. We did not uncover any specific reference to this in our review.

ETIOLOGIC MECHANISMS IN THE DEVELOPMENT OF COLLATERAL CIRCULATION

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ALTHOUGH the importance of collateral circulation has long been recognized, the exact mechanism for its development has not been clearly defined. This report is concerned with some observations on the relative roles of pressure and anoxia in the development of collateral circulation and the application of these findings in clinical cases of occlusive peripheral vascular disease.

MATERIALS AND METHODS

A total of 93 extremity preparations were used in 49 mongrel dogs. For the clinical aspects of the report 31 patients with occlusive peripheral vascular disease were studied.

The dogs were anesthetized with pentobarbital in dosages of 60 mg. per kilogram of body weight administered intravenously. Simultaneous pressure pulses were recorded at the common femoral and anterior tibial arteries of the dog by means of No. 20 gauge needles, transducers, and a recording amplifier. The superficial femoral artery was occluded at the distal end of the adductor canal. Seventy per cent Hypaque was used in repeated arteriograms and cinefluorograms before and during the course of acute occlusion. Changes in tissue pO_2 were recorded in the calf muscle by means of a bare platinum tip electrode with a fixed negative potential of 0.6 volts DC with standard circuits.[2, 11, 16]

In order to evaluate the relative roles of anoxia and pressure changes in the development of collateral circulation, the superficial femoral artery distal to the site of occlusion was perfused on separate occasions with unoxygenated blood obtained from the inferior vena cava and oxygenated blood prepared in a bubble oxygenator. Perfusion was begun at the moment of occlusion with a pressure corresponding to that in the anterior tibial artery.

In the clinical cases arteriograms before and after operation were performed by standard techniques. Intra-arterial pressure tracings were obtained before and after operation at selected sites above and below areas of occlusion. In cases of aortoiliac occlusive disease pressure tracings were usually obtained in the proximal aorta and in the superficial femoral and anterior tibial arteries. In cases of occlusion of the superficial femoral artery pressure tracings were usually made in the common femoral, the popliteal, and the anterior tibial arteries.

RESULTS

Pressure recordings before and after occlusion were obtained in 66 experiments on 33 dogs. Following acute occlusion of the superficial femoral artery at the distal end of the adductor canal, a drop in arterial pressure to a nonpulsatile level between 35 and 60 mm. Hg was noted (Fig. 1). A feebly pulsatile

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pressure pulse contour was observed to begin within 4 to 6 seconds. Subsequently, there was a progressive increase in systolic, diastolic, and pulse pressure, and in the majority of animals at the end of one minute of occlusion the anterior tibial artery pulse pressure was 14 to 16 mm. Hg, and the systolic pressure was approximately equal to the diastolic pressure before occlusion.

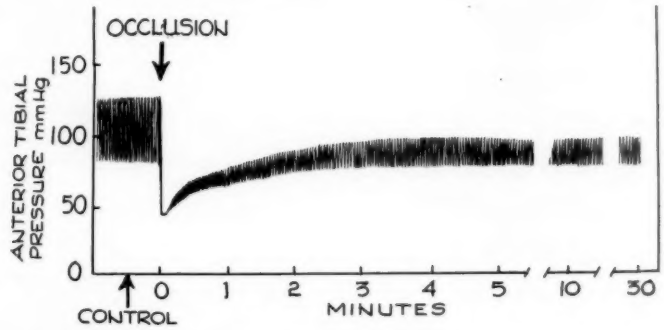


Fig. 1.—This drawing demonstrates the typical changes occurring in the anterior tibial artery pressure pulse following occlusion of the superficial femoral artery. The common femoral pressure tracing proximal to the occlusion showed no change. The anterior tibial pressure fell abruptly at the time of occlusion, and a nonpulsatile area of the curve was noted for a few seconds following occlusion. Subsequently the anterior tibial pressure rose to reach a maximal level at approximately 4 minutes following occlusion and showed essentially no change in systolic, diastolic, or pulse pressure for intervals up to 4 months.

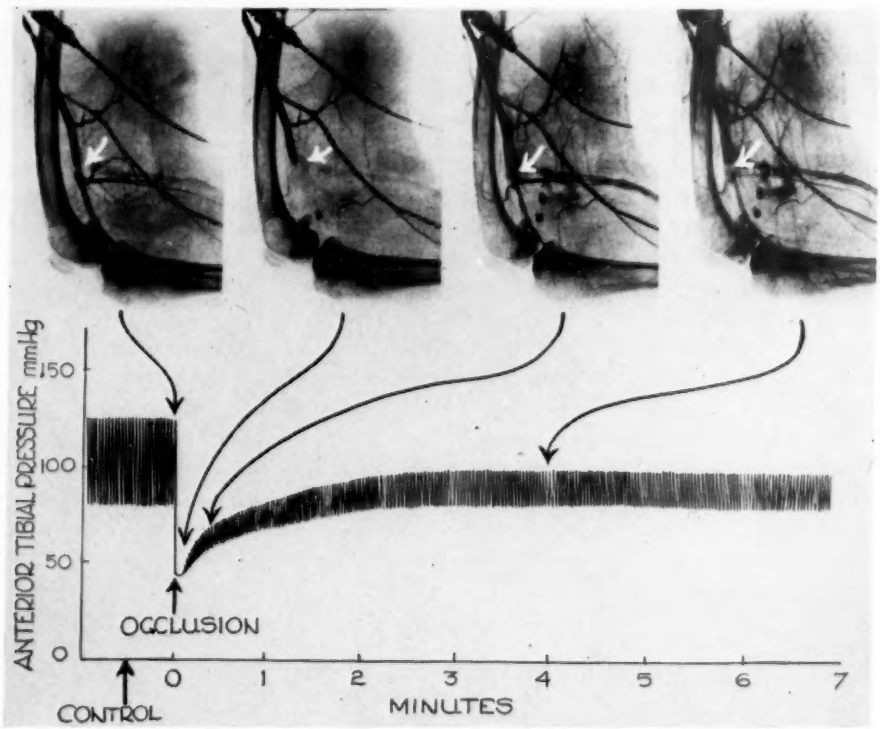


Fig. 2.—The characteristic changes demonstrated in serial arteriograms following acute occlusion are correlated with simultaneous anterior tibial artery pressure pulse tracings.

Thereafter there was a slower rise in systolic, diastolic, and pulse pressures. The interval between occlusion and development of maximal anterior tibial pressure ranged from 2 to 8 minutes with an average of about 4 minutes. The

pulse pressure varied from 16 to 24 mm. Hg and the systolic pressure always exceeded the preocclusion diastolic pressure. These maximal pressures were maintained for as long as 4 months after occlusion.

Fluoroscopy, cinefluorography, and serial x-rays were used to correlate the development of collateral channels with intra-arterial pressure tracings. Collateral vessels could be demonstrated arising from the femoral artery proximal to the site of occlusion during the initial nonpulsatile portion of the anterior tibial pressure tracings (Fig. 2). As the pressure became pulsatile, collateral vessels originating proximal to the site of occlusion were observed to communicate with vessels joining the artery distal to occlusion. The development of collateral vessels by angiography appeared to vary directly with the increase in anterior tibial pressure. It was concluded, therefore, that alterations of arterial pressure pulses toward normal distal to the site of acute occlusion represent the opening of collateral pathways (Fig. 2).

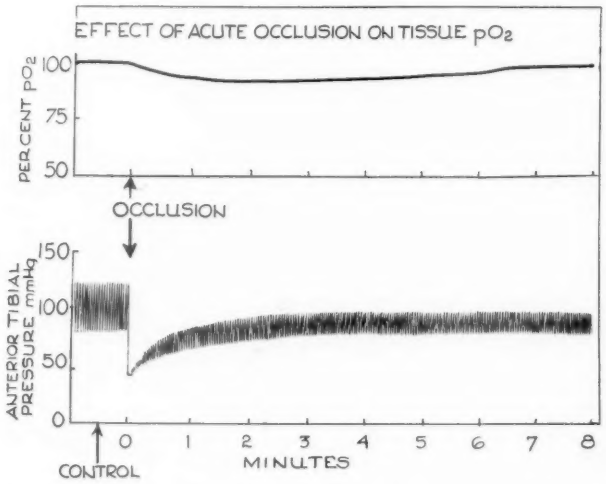


Fig. 3.—The characteristic changes in tissue pO_2 measured in the calf muscle following acute occlusion are correlated here with simultaneous anterior tibial artery pressure pulse tracings.

The effect of acute occlusion on tissue pO_2 was investigated in 14 experiments on 7 dogs. Following occlusion the tissue pO_2 in the calf muscle decreased to a mean minimum of 90 per cent of the control level, with a range of 84 to 95 per cent. Thereafter, the pO_2 slowly rose to reach control values within 5 to 8 minutes (Fig. 3).

Perfusion of the superficial femoral artery distal to the site of acute occlusion with saturated and unsaturated blood at anterior tibial pressure was performed in 10 experiments on 6 dogs. Perfusion was begun coincident with occlusion, but no significant difference from the response obtained following acute occlusion alone was noted (Fig. 4).

In the series of 31 clinical cases angiograms and multiple intra-arterial pressure pulse tracings were recorded before and after operation for correction of vascular occlusion. In most instances pressure tracings were obtained proximal to the site of occlusion and at various levels distally. In cases of

aortoiliac occlusive disease, pressure pulses were recorded in the aorta, the superficial femoral, and the dorsalis pedis arteries. In cases of iliofemoral occlusion, pressure pulses were recorded in the aorta and in the femoral, popliteal, and dorsalis pedis or posterior tibial arteries. In cases of occlusive disease of the superficial femoral artery, pressure pulse tracings were made in the femoral vessel proximal to occlusion and in the popliteal and dorsalis pedis or posterior tibial arteries.

In cases of aortoiliac occlusion a marked fall in pressure was noted between aorta and the superficial femoral artery. Generally the femoral pressure was of a moderately high level and was feebly pulsatile. Pressure tracings in the dorsalis pedis artery were generally of the same pressure level and pulse contour as the femoral tracings. Following surgical restoration of adequate blood flow by either resection and replacement or bypass procedures, the intra-arterial tracings in the femoral and the dorsalis pedis vessels showed essentially normal pressure levels and pulse contours (Fig. 5).

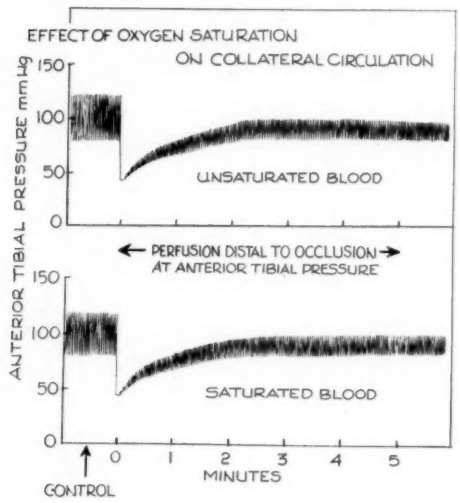


Fig. 4.—The responses in the anterior tibial pressure pulse tracing to acute occlusion was not altered by perfusion with saturated or unsaturated blood.

In cases of iliofemoral occlusion, moderate decreases in pressure were generally noted between aorta and femoral arteries and between the femoral and popliteal arteries. The femoral pressure was generally at a moderate level and weakly pulsatile whereas pressure in the popliteal and dorsalis pedis was generally at a lower level and also weakly pulsatile. Following aorto-femoral bypass procedures, pressures in the popliteal and dorsalis pedis were found to be essentially normal; however, in one case, pressure in the femoral artery which lay between two sites of occlusion was found to be slightly subnormal (Fig. 6).

In the majority of cases of superficial femoral artery occlusion, a moderate decrease in pressure was noted between the proximal femoral and the popliteal arteries, and no further decrease in pressure was apparent in the foot. The popliteal artery pressure was generally of a moderate level, ranging from 45 to 92 mm. Hg and was weakly pulsatile. The distal pressure pulses showed the

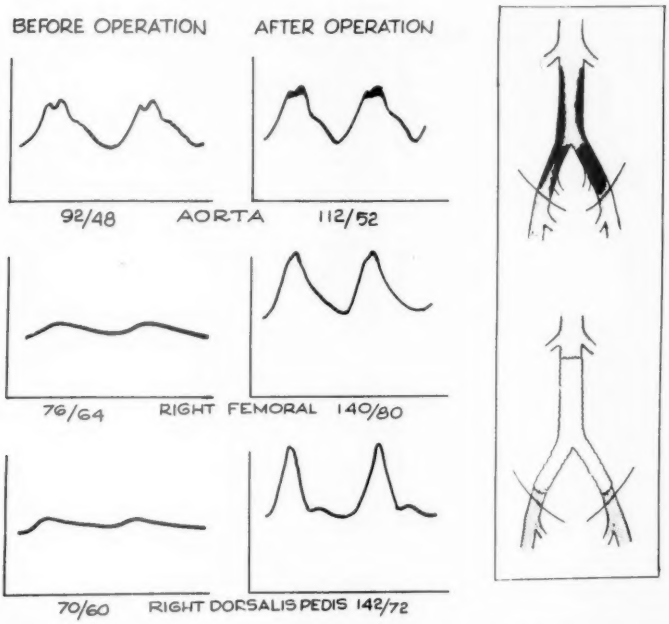


Fig. 5.—Preoperative pressure pulse tracings showed the femoral pressure to be somewhat lower than the aortic level and feebly pulsatile. The dorsalis pedis pulse tracing is essentially the same as the femoral. Following operation normal pressure levels and pulse contours are noted in both femoral and dorsalis pedis pulse tracings.

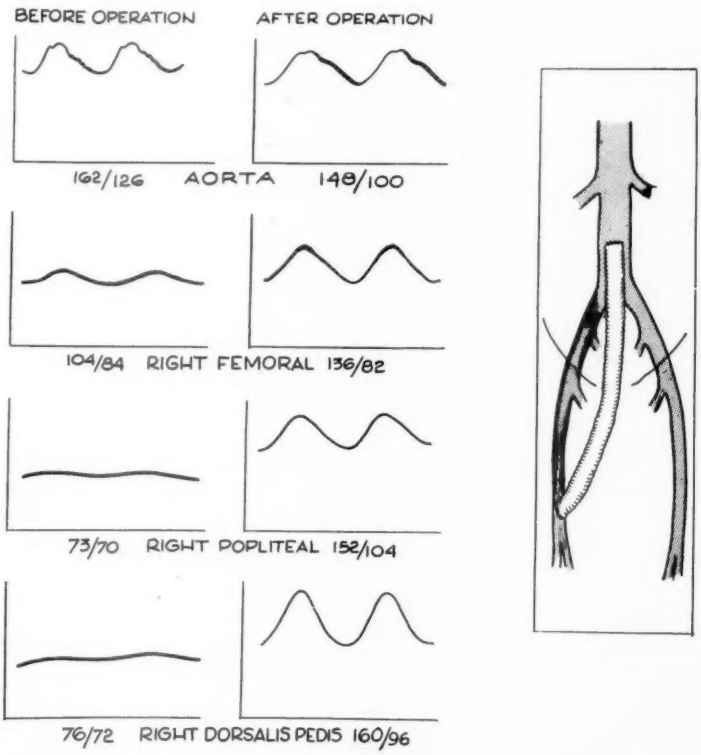
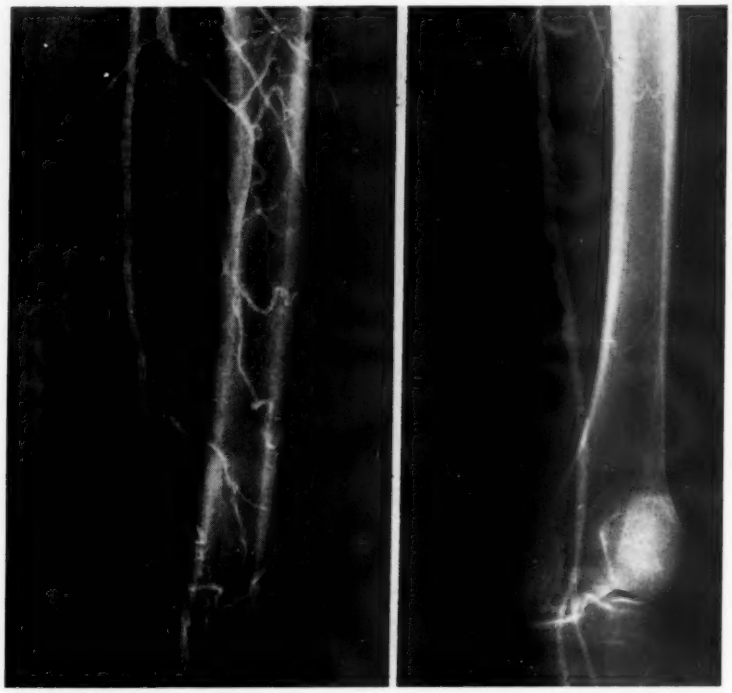
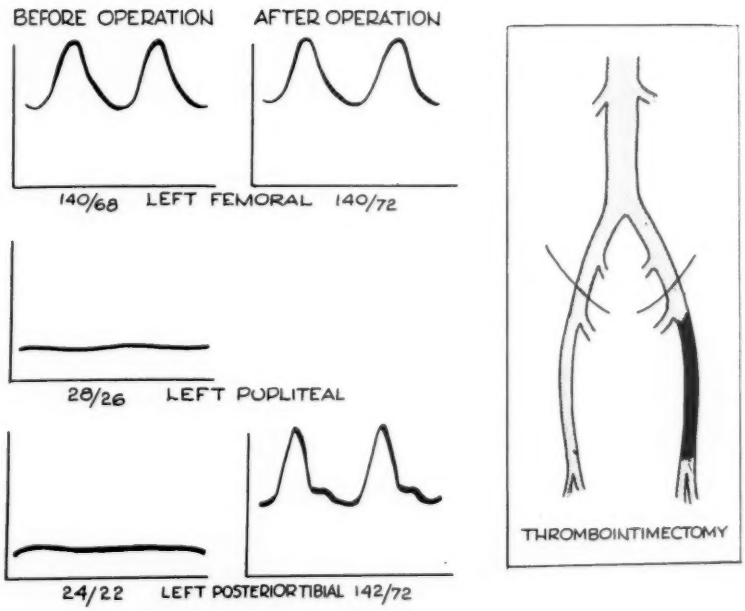


Fig. 6.—In a case of iliofemoral occlusion tracings before operation showed a moderate reduction in pressure between the aorta and the femoral artery. A further decrease was noted in the popliteal artery; however, pressure in the dorsalis pedis was essentially equal to that in the popliteal. Following a bypass procedure, as diagrammed above, pressure in the popliteal and dorsalis pedis arteries returned essentially to normal levels. However, pressure in a portion of the femoral artery which lay between two sites of occlusion remained somewhat subnormal.



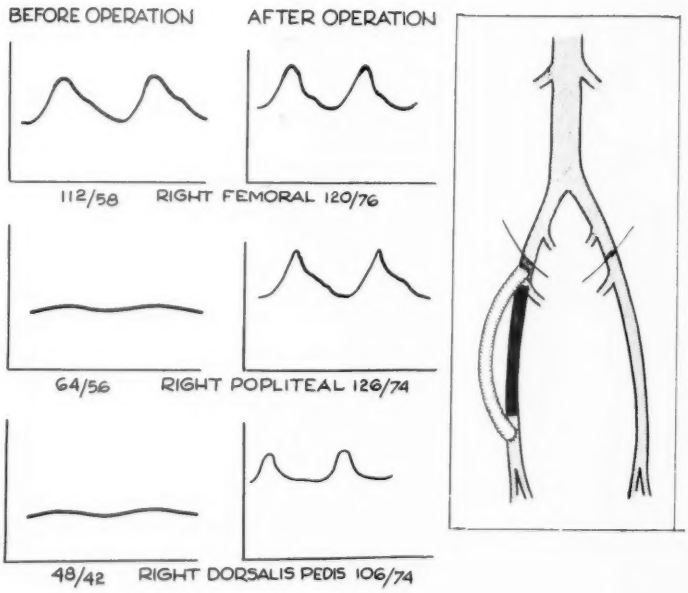
A.



B.

Fig. 7.—*A*, Angiograms before and 7 hours after thrombointimectomy for segmental occlusion of the left superficial femoral artery. *B*, Pressure pulse tracings in the case shown in *A*. A marked drop-off was noted between femoral and popliteal arteries; however, the posterior tibial pressure was essentially equal to that in the popliteal. Following surgical correction a normal posterior tibial pressure pulse was noted.

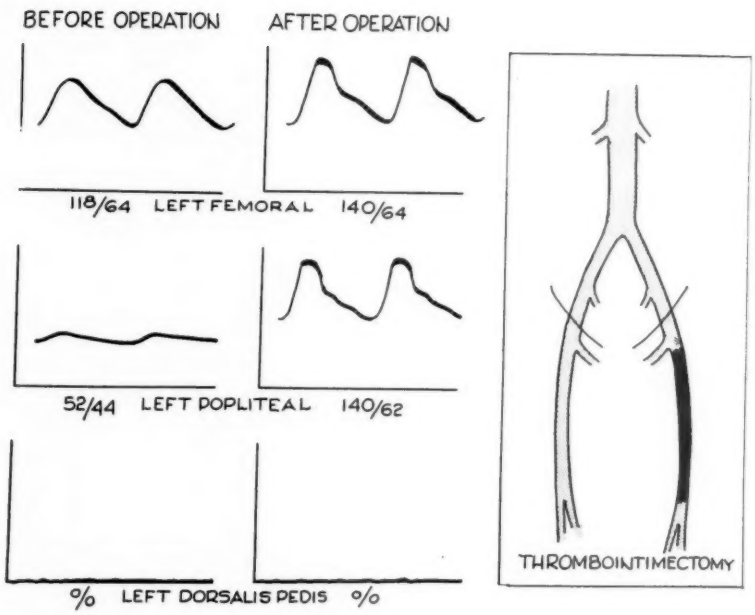
A.



B.

Fig. 8.—*A*, Angiograms before and 6 hours after a bypass procedure for segmental occlusion of the right superficial femoral artery. *B*, Pressure tracings in the case shown in *A* demonstrated a moderate drop-off between femoral artery and popliteal artery pressures. The further drop-off in dorsalis pedis pressure suggested obstruction distal to the popliteal artery. Postoperative tracings showed an improved but still subnormal dorsalis pedis artery pressure.

A.



B.

Fig. 9.—*A*, Angiogram before thrombointimectomy for segmental femoral artery occlusion. *B*, Pressure tracings in the case shown in *A* revealed a moderate fall in pressure between femoral and popliteal arteries and a further fall between popliteal and dorsalis pedis. Postoperative tracings showed a normal popliteal level but an unchanged pressure in the dorsalis pedis, suggesting obstruction between the popliteal and dorsalis pedis levels.

same characteristics. In all these cases following restoration of adequate blood flow by either thrombointimectomy or bypass procedures, the popliteal and foot pressure pulses returned to a normal level and contour. For example, an arteriogram prior to thrombointimectomy for segmental occlusion of the superficial artery (Fig. 7, *A*) disclosed several large collateral vessels bridging the occluded segment. Pressure pulses recorded in the common femoral, popliteal, and posterior tibial arteries indicated a decrease in pressure from femoral to popliteal arteries but no further drop in pressure in the pedal arteries (Fig. 7, *B*). About 7 hours after operation the arteriogram and pressure pulse tracings were repeated. It was observed that collateral vessels had undergone such marked decrease in size that they were hardly visible (Fig. 7, *A*). Pressure pulses in the posterior tibial artery were restored to normal (Fig. 7, *B*). A similar pattern of response was observed in a case of segmental femoral artery occlusion in which a bypass procedure was performed (Fig. 8, *A* and *B*). However, in this case the decrease in pressure preoperatively between popliteal and dorsalis pedis arteries suggested obstruction below the popliteal level. Following operation, the pedal pulse was improved but remained subnormal. In another case (Fig. 9, *A* and *B*) the marked drop in pressure between popliteal and pedal pressures suggested extensive involvement below the obstruction. Following thrombointimectomy, the popliteal pressure returned to normal but the pedal pressure remained unchanged. Although the foot remained viable, ischemic symptoms persisted.

DISCUSSION

Perhaps the earliest recorded observations on the importance of collateral circulation were made by Antyllus,[1] who noted that ligation of the major vessel to an extremity did not invariably result in gangrene. Experimental studies on the development of collateral circulation began with the classic work of John Hunter,[9] who observed that ligation of the main vessel to the growing antler of the deer was followed by the rapid appearance of many enlarged vessels around the site of obstruction. The importance of the pressure gradient proximal and distal to the site of occlusion was first suggested by Von Recklinghausen[21] and subsequently by Nothnagel[18] and Matas.[15] Another theory involving pressure gradients was developed by Weber,[22] who suggested that the pressure proximal to the site of occlusion was increased sufficiently to cause increased flow through collateral vessels.

The concept that the accumulation of metabolites in an area of ischemia might be responsible for the development of collaterals was initially advanced by Latschenberger and Deahna[13] and later amplified by Lewis.[14] The theory of "tissue needs" was advanced by Reid.[19] The observation that the experimentally denervated extremity in the salamander, frog, and pigeon was followed by gangrene after ligation of the major vessel led Stefani[20] to propose that the ischemia distal to the site of occlusion caused reflex vasodilatation and development of collaterals. The importance of reflex action in the development of collaterals was also suggested by Halsted.[4] On the basis of a striking temperature elevation of the hand and forearm following excision of

a subclavian aneurysm and ligation of the subclavian and axillary arteries, Halsted concluded that the division of periarterial sympathetics was responsible for the development of collateral flow. The importance of periarterial sympathetics was further suggested by the studies of Kolesnikow,[12] who observed that alcohol injection of the adventitia of major blood vessels resulted in increased collateral circulation. Further evidence for vasomotor components in the development of collateral circulation was presented by Mulvihill and Harvey,[17] who noted that lumbar sympathectomy prevented the abrupt fall in temperature occurring following ligation of the external iliac artery of a dog.

The importance of pressure gradients in the development of collateral vessels was emphasized by the classic studies of Holman[5, 6] on the physiology of arteriovenous fistulas. More recently, in studies on ligation of large vessels, Holman[7, 8] has further emphasized the importance of pressure gradients, the transformation of end pressure to lateral pressure in an occluded vessel, and the direction of flow through arteriolar beds.

The development of collateral circulation following acute occlusion of major vessels were studied by Eckstein, Gregg, and Pritchard.[3] These investigators concluded that the development of collateral circulation was influenced by a number of factors including "differential pressure, metabolites, nerve action, and formation of new vessels." The effects of restoration of arterial flow on existing collaterals were reported by Jacobson and McAllister.[10]

This study was undertaken to evaluate the role of some of the etiologic factors in the development of collateral circulation. It was observed that following acute occlusion of the superficial femoral artery in the dog the pressure proximal to the site of occlusion did not rise. Furthermore, a drop in pressure distal to the site of occlusion to a nonpulsatile level between 35 and 60 mm. Hg was consistently noted. During the first 4 to 6 seconds following acute occlusion a marked pressure gradient existed across to the site of occlusion.

It was observed by arteriography and cinefluorography that collateral flow developed simultaneously with the onset of occlusion. Within the first 4 to 6 seconds after occlusion, when the distal pressure was nonpulsatile, collateral vessels were seen to arise from the major vessel and its branches proximal to the site of occlusion. Approximately 6 seconds after occlusion, when the pulse contour in the distal vessel was noted to become pulsatile, collateral vessels originating proximal to the site of occlusion were noted to communicate with similar vessels which joined the arterial trunk distal to the site of occlusion. Within 3 to 5 minutes following occlusion, when the anterior tibial pressure reached a maximal level, the collateral circulation as shown by arteriograms and cinefluorograms also was maximal.

The next etiologic mechanism which was investigated in the development of collateral circulation was anoxia of the tissues distal to the site of occlusion. The maximal drop in tissue pO_2 was noted approximately one minute following acute occlusion, whereas maximal fall in pressure was noted instantaneously

(Fig. 3). Perhaps this discrepancy may be partially explained by the prolonged equilibration time of the bare platinum electrode which was used to record tissue pO_2. In order to evaluate the importance of anoxia in the development of collateral circulation, an experiment was devised to perfuse the extremity distal to the site of occlusion with saturated and unsaturated blood on different occasions, and under these conditions no effect on the development of collaterals was noted (Fig. 4).

The clinical studies support these experimental observations. Thus, in the presence of a significant pressure gradient across an area of obstruction, an extensive collateral network functions to bridge the obstructed segment. Restoration of blood flow and pressure by thrombointimectomy or bypass causes a rapid decrease in size of these collateral vessels. Furthermore, the intra-arterial pressure tracing obtained distal to an obstructed segment appears to be correlated with the size of collaterals. In fact, such tracings have frequently proved to be better guides of collateral circulation than have arteriograms. In general, patients who showed high pressure (75 to 90 mm. Hg) in the pedal arteries have been found to have excellent runoff. When the pedal artery pressure was low (15 to 50 mm. Hg), another tracing was made immediately below the level of occlusion. In such cases when the pressures just distal to occlusion are approximately equal to the pressure in the foot the runoff has proved to be adequate (Fig. 7, *B*). However, in cases which show a significant drop in pressure between the area just distal to occlusion and the foot, the runoff appears to be impaired (Figs. 8, *B* and 9, *B*).

SUMMARY

1. The development of collateral circulation in humans and in dogs has been studied by intra-arterial pressure tracings, arteriography, cinefluorography, tissue pO_2, and in the dog with perfusion of a major artery distal to occlusion with saturated and unsaturated blood.

2. The development of collateral circulation in the dog, as measured by arteriography and distal pressure tracings, appears to correspond directly with the pressure gradient at the site of occlusion. Perfusion of the extremity distal to occlusion with saturated and unsaturated blood produced no appreciable effect on the development of collateral circulation.

3. The use of pressure pulse tracings and arteriography in clinical cases have confirmed the experimental observations that pressure gradients are a determinant of collateral flow.

4. The use of pressure pulse tracings in clinical cases has proved to be a valuable adjunct in the diagnosis and selection for operation of cases of occlusive peripheral vascular disease. Preliminary studies suggest that such pressure tracings are frequently superior to arteriography in the assessment of the areas of runoff.

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DISCUSSION

DR. EMILE F. HOLMAN (San Francisco, Calif.).—I am very grateful for these very exact studies which corroborate some of the things that we have talked about in the past. I could never accept Sir Thomas Lewis' concept of collateral circulation as being a response to some tissue substance produced in an avascular area which acted upon the blood vessels to this area to dilate them. It seems more logical to assume that blood like water flows to the point of least resistance, a concept that is being corroborated in these very beautiful studies on collateral circulation. It is not only true in the systemic circulation but, as you heard this morning, in the pulmonary circulation. Flowing blood, like flowing water, will inevitably follow the line of least resistance.

DR. HENRY HAIMOVICI (New York, N. Y.).—For some years we have been interested in the study of arterial hemodynamics in segmental occlusive arterial disease (SURGERY **36:** 1075, 1954; A. M. A. Arch. Surg. **72:** 107, 1956). Simultaneous arterial pressure recordings in the common femoral and popliteal arteries before and after bypass grafting for segmental femoral occlusion may be of great value in assessing the effectiveness of the available preoperative collateral circulation and the degree of restoration of the pulsatile flow in the distal major artery after the implantation of the graft.

In support of Dr. Winblad and his associates' presentation, I should like to show some of our findings of arterial pressure recordings as illustrated in two slides. In the first slide, arterial pressure recordings are shown before and after a bypass implantation of an Edwards-Tapp nylon graft from the common femoral to the upper popliteal artery. It is noteworthy that before implantation of the graft, for spreading gangrene of the foot in a 74-year-old man, the popliteal arterial pressure was nonpulsatile and measured 50 mm. Hg. Immediately following the insertion of the graft, the pulse pressure curve exhibited a normal contour and measured 120/45 mm. Hg as compared to 130/50 mm. Hg in the common femoral artery. The second slide illustrates a similar situation to the previous case, except that the popliteal pressure before implantation of the graft was slightly pulsatile and measured 82/65 mm. Hg. In this instance, there was marked intermittent claudication without trophic changes. After insertion of the graft, again the popliteal arterial pressure exhibited a normal pulsatile curve with a pulse pressure of 45 mm. Hg, which is a significant increase from the 17 mm. Hg present before. In both of these cases, however, after restoration of the arterial flow, the popliteal arterial pressure did not equal that in the common femoral. This appears to be at slight variance with the results presented by Dr. Winblad and his associates. Perhaps some degree of stenosis of the popliteal artery may account for this difference in our cases.

DR. CREECH (closing).—We believe the significance of this study lies in the fact that it confirms Dr. Holman's observations that collateral circulation is developed through a simple mechanistic action. A fact not widely recognized is that collateral vessels apparently do not form after long intervals of occlusion, but rather they are present continuously and do not function because of the lack of a pressure gradient. An additional fact is that they begin to function immediately when a pressure gradient is created, and they cease to function when that gradient is eliminated by restoration of blood flow. The clinical implications are difficult to evaluate, but certainly some patients who have had segmental occlusion relieved by bypass procedures or thrombointimectomy and who subsequently developed acute occlusion have developed severe ischemia because their collaterals had regressed during the interval when blood flow was restored.

THE USE OF DIGITAL PULSE RECORDING IN VASCULAR DISEASE

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INTRODUCTION

EVALUATION of the state of the arterial circulation in limbs of patients with vascular disease will always primarily depend upon the history and physical examination. More information is nearly always desirable and for this reason arteriography, vasodilatation tests, and oscillometry are widely used methods of study. None of these, however, allows continuous evaluation of the rapid changes in peripheral circulation which occur over a period of seconds or minutes.

For example, the vascular spasm which sometimes follows dye injection may be of serious consequence, particularly in studies of the cerebral circulation. Although the danger of serious sequelae resulting from femoral arteriograms is less than that following cerebral arteriograms, it seemed that a survey of the rapid changes in peripheral circulation which might be expected following even relatively innocuous dye injection would be interesting and useful. Digital plethysmography is the most precise method of evaluating rapid changes in peripheral circulation but is somewhat impractical for routine use on a surgical service and in operating rooms. During the past year, we have been using a simple, sensitive, electronic pickup to record in a semiquantitative manner the amplitude and contour of digital pulses in a variety of clinical conditions. This instrument was developed in Germany,[1] and has been used there[3] and to a lesser extent in this country.[18] It consists of two pulse pickup units or transducers, a control box,* and any standard two channel electrocardiograph machine.† Fig. 1 shows the manner in which the pickups are applied. Each pickup is attached to the end of the distal phalanx of a digit with cellulose tape, or it may be placed over an artery such as the radial with a strap or with tape. The small force generated by the pulse is transformed into a corresponding voltage by a variable capacitance within the pickup unit and by the control box and is amplified and recorded on paper by the electrocardiograph machine.

This study was supported in part by the Hartford Foundation and in part by the Heart Association of Southeastern Pennsylvania.

Read at the Twelfth Annual Meeting of the Society for Vascular Surgery, San Francisco, Calif., June 22, 1958.

*Infraton Model B pickups and Model AR control unit manufactured by Medical Electronics Development Company, Great Neck, L. I., N. Y.

†Sanborn Twin-Viso Cardiette and Elema Mingograf 24 were used.

The instrument is sufficiently sensitive to have demonstrated repeatedly a pulse in patients' toes even when no pulse was palpable in the limb and when oscillometer readings were zero. It will more quickly inform the observer of any change or loss of pulse than is possible by palpation.

The study of peripheral arterial pulses with recording instruments has been carried on in increasing detail since the time of Marey, who by 1860 had utilized a spring to transmit motion from a button overlying an artery to a recording lever. Better instruments were developed for the same purpose in the early part of this century, largely by European physiologists. Ohm (1910) recorded the radial pulse using a mirror cemented to the skin overlying the radial artery. A practical segment-capsule device, which increased accuracy by using optical rather than mechanical levers, was developed by Frank and later modified by Wiggers.[20] A great amount of work has been done by clinicians, physiologists, and mathematicians in interpreting the shape of peripheral pulses recorded with such devices. Both Sir James MacKenzie and

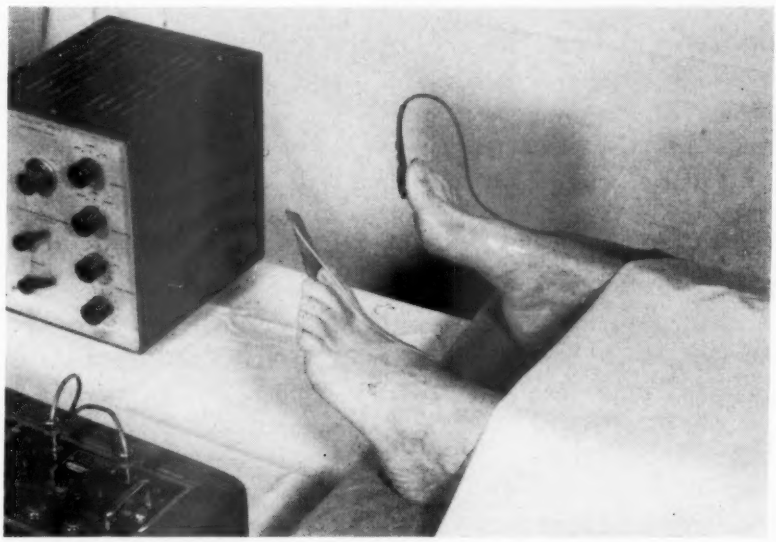


Fig. 1.—Method of obtaining digital pulses. The pickup units are mounted on each large toe with cellulose tape. Wire runs from each pickup to the control box which is connected to the recording electrocardiograph machine.

Sir Thomas Lewis made contributions to the development of recording instruments and used them in the study of cardiac arrhythmias.[13, 14] Bramwell in 1937[2] and Wiggers in 1952[19] summarized for clinicians the then current ideas regarding interpretation of the arterial pulse. The intervening years have been marked by rapidly accelerating use of intra-arterial methods of blood pressure and pulse wave study. Other investigators in the present decade have shown that complex, dynamic factors involved in motion of blood and arterial walls make exact interpretation of the pulse amplitude and contour very difficult, even in normal subjects.[5, 12, 16, 17] Needle puncture of distal peripheral arteries in patients with arteriosclerotic and other vascular diseases cannot be performed freely nor repeatedly with safety, and therefore the accumulation of information concerning peripheral pulse wave shape and timing has continued using

external pickup methods as well as intra-arterial methods.[10, 11] Interpretation of the mechanisms by which the central aortic pulse becomes transformed to the peripheral pulse has become a very active field of study, involving calculations that warrant the use of electronic computers.[22]

The pulse wave in the digits, as contrasted with that in the large peripheral arteries, was first recorded by Muller and Weis in 1911.[15] Studies comparing the forms of the pulse waves in the radial artery and in the digits were made by a number of German and Japanese investigators in the nineteen thirties, and by Dillon and Hertzman in this country in 1940-1941.[7] The latter authors pointed out that "it is well known that the pulse becomes more dicrotic in fever, and that, in arteriosclerosis, secondary waves on the dicrotic limb become obliterated, and the peak of the wave becomes rounded." From their study, they concluded that in arteriosclerosis and hypertension, the contour of the digital pulse is altered earlier and to a greater extent than the contour of the radial artery pulse. Using plethysmographic techniques, a number of investigators have shown that pulse pressure is reduced proportionately more than is the mean pressure by an arteriosclerotic block.[8] Digital plethysmographs have been developed into useful instruments and have been used for investigation by Burch,[4] Winsor,[21] and others. They also have been used in evaluation of the results of operative vascular procedures. It has been shown by this method that sympathectomy usually increases digital flow more than it increases the digital pulse,[21] and also that unsuccessful bypass grafts may reduce digital blood flow, even though collateral vessels are minimally disturbed at the time of operation.[6]

With the externally placed transducer mentioned we observed rapid pulse changes during certain vascular procedures and obtained records demonstrating changes in pulse wave form produced by removal of arterial obstruction.

METHOD

The transducers are applied as described above. Care should be taken not to constrict ischemic toes nor to leave the pickups in place for long periods on ischemic toes. Placement on the pad of the finger or toe is not critical. More care is required in placement for recording radial artery pulses. For these the pickup must be held directly over the artery with a strap or with tape. Artifacts frequently occur in dorsalis pedis artery records due to motion of adjacent tendons and will be introduced into any record by motion of the limb or digit.

Records made with the pickup unit held on the skin overlying the radial artery closely approximate in contour records made using a needle in the radial artery and intra-arterial recording techniques. Fig. 2 shows the pulse recorded simultaneously from a healthy adult's left radial artery, using the external pickup and from his right radial artery using standard intra-arterial recording equipment.* The onset of the two waves is nearly simultaneous, but the peak in the record made with the external pickup is delayed approximately 0.04 second. This delay presumably is due to the damping effects of the arterial wall, subcutaneous tissue, and skin. Although the two curves are not identical, they are closely similar and indicate that records made with the external pickup are adequate for our purposes.

*Sanborn 467-B Transducer, 150-1100 carrier preamplifier, 64-300 DC amplifier, and Twin-Viso writer.

Our records have usually been made from the large toe or long finger of the limb in question and simultaneously from the similar digit of the contralateral limb which acts as a control. Normal finger and toe pulse curves have quite different contours, as is illustrated in Fig. 3.

INTERPRETATION

The factors involved in interpretation of digital pulses in this study are simple.

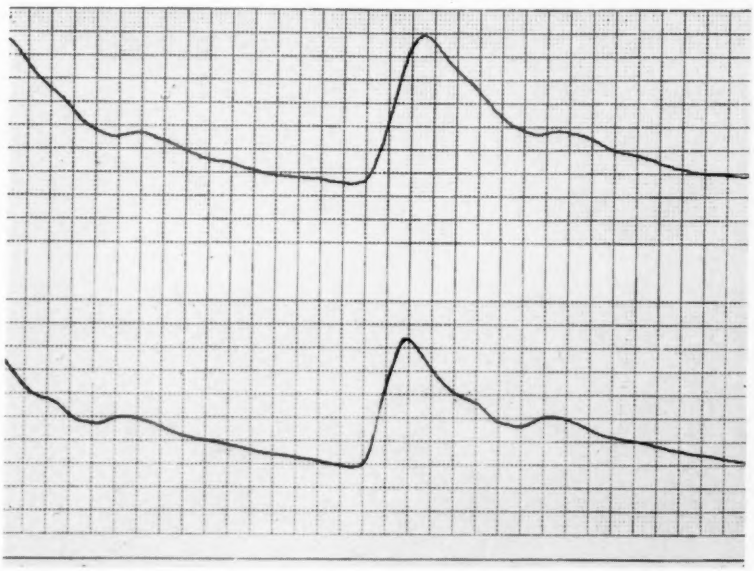


Fig. 2.—Radial artery pulse curves. Upper record made with external pickup applied over left radial artery; lower record made with a No. 20 needle inserted into right radial artery and connected to standard intra-arterial pressure apparatus. Note time differences in peaks but also general similarity of the two curves.

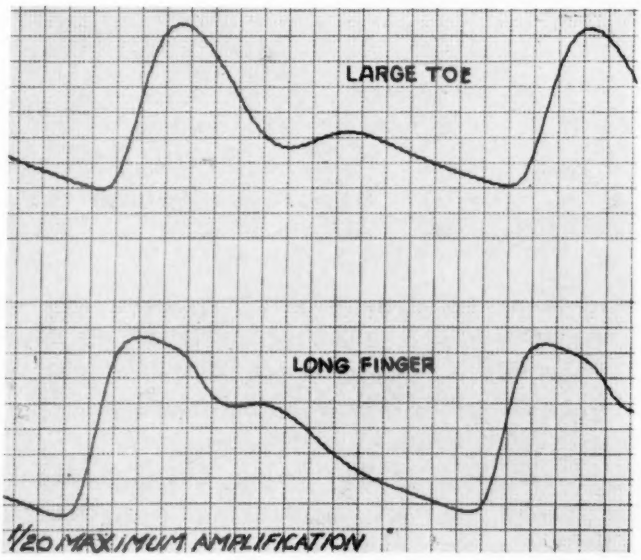


Fig. 3.—Normal digital pulses recorded with the external pickup. Note differences in contour of toe and long finger curves. Each is amplified only one twentieth of maximum. Compare with Fig. 4.

Amplitude of the pulse in the digits may be easily classified into broad categories of high normal, low normal, definitely subnormal, or nearly absent. Knowledge of the circumstances under which the record was made, such as room temperature plus comparison of the pulse in the digit in question with pulses in digits of other limbs makes clear whether a reduction in pulse amplitude is general or local. When considered in a strict sense, amplitudes of the recorded digital pulse waves represent changes in the force which the digit exerts on the transducer during each pulse cycle. Such records represent in a semiquantitative manner the pulsatile element of digital blood flow.

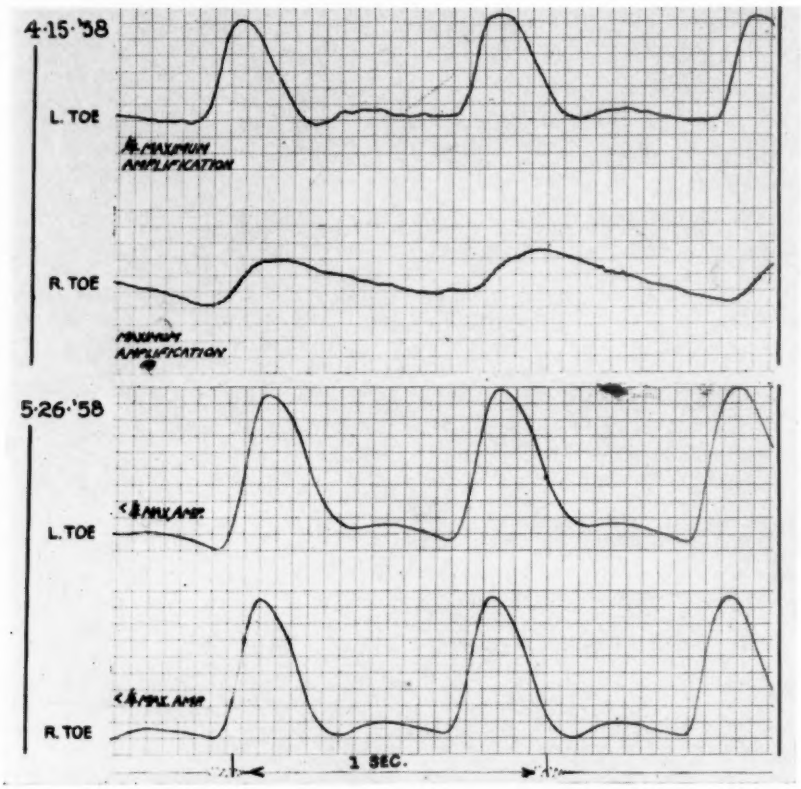


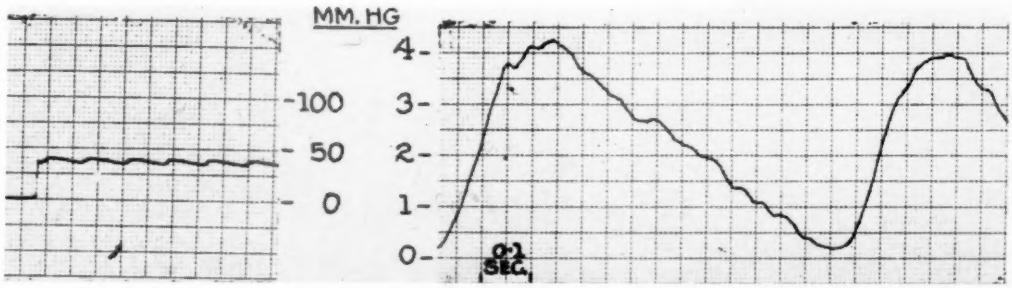
Fig. 4.—Left and right toe pulses before (*above*) and after (*below*) removal of an obstruction in the right superficial femoral artery by endarterectomy. The right toe pulse regained normal contour and amplitude. This patient had had an autogenous saphenous vein segment inserted in his left femoral artery 4 years prior to the time this record was made.

Timing of the onset and of the peak amplitude of the pulse in one digit compared to its counterpart is a second useful factor in interpretation of these records. Onset and peak of the digital pulse are delayed when obstruction reduces the rate of pressure increase and when blood must pass through small or lengthy collateral channels.

The *contour* of the pulse is the third factor useful in evaluation. The contour is definitely abnormal when it exhibits no dicrotic wave, and in addition is "saw-toothed" or triangular in form. Fig. 3 illustrates normal contours of the finger and toe pulses. Fig. 4 shows a left toe pulse of normal contour and amplitude and for comparison a right toe pulse which is subnormal in amplitude, delayed in time, and abnormal in contour.

ILLUSTRATIVE CASES

Fig. 4 also illustrates the change in toe-pulse shape produced by removal of an obstruction in the right superficial femoral artery; femoral endarterectomy had been performed on the right side during the interval between these two recordings. In addition, normal variations in pulse amplitude associated with changes in environmental temperature are illustrated by these two records. The upper record was made under relatively cool conditions and the later lower one in a warm room. It is also of interest that this patient had an autogenous saphenous vein segment placed in his left femoral artery for relief of obstruction nearly 4 years before. These records clearly demonstrate prolonged maintenance of normal pulse amplitude and contour following placement of an autogenous vein in the left femoral artery and return to normal amplitude and form following right femoral endarterectomy. Fig. 5 is a record from the same patient of intra-arterial pressure in the right superficial femoral artery, below the point of obstruction, made just before endarterectomy in this patient. The pulse pressure in the artery below the block was less than 5 mm. Hg, which is unusually low in our experience, yet the transducer on the toe was sufficiently sensitive to record a digital pulse.



A. *B.*

Fig. 5.—Same patient as Fig. 4, showing (*A*) intra-arterial pressure and (*B*) amplified pulse wave form in the right superficial femoral artery below the block prior to its removal.

Fig. 6 illustrates the total although transient loss of the pulse in a toe following injection of 20 c.c. of a 35 per cent solution of Hypaque for a femoral arteriogram. The irregularities in the record during the time the pulse was absent are artifacts due to motion of the patient's leg. That the loss of the pulse was due to spasm is clearly demonstrated by the return of the pulse in this patient after several minutes and following intra-arterial injection of procaine. This degree of spasm, in our experience, has usually been accompanied by severe pain, which the patient had.

Fig. 7 shows records made during popliteal embolectomy and illustrates an immediate change in circulation before clinical signs were apparent. This patient had had an abdominal aneurysm resected and replaced with a homograft approximately 10 hours before embolectomy was performed. Following excision of the aneurysm the large toe pulse disappeared. When the embolus was removed the pulse returned. This return gave an immediate indication that there was then no complete occlusion at more distal levels than the popliteal.

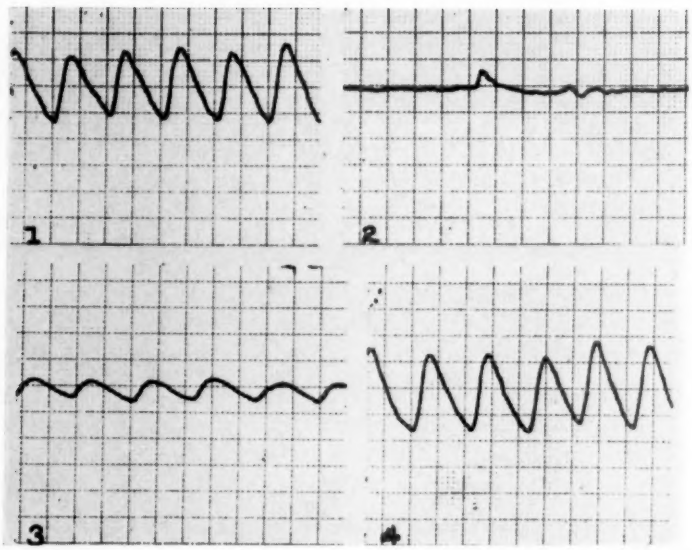
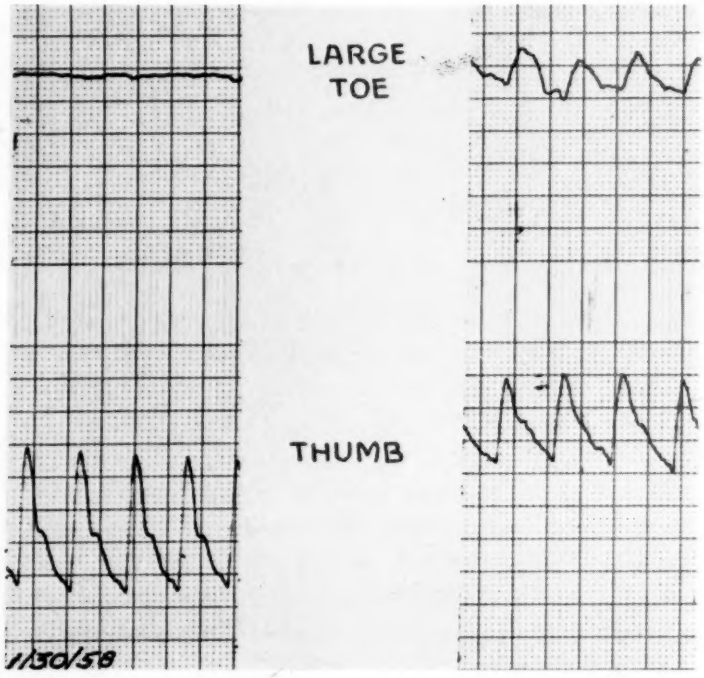


Fig. 6.—Temporary loss of the large toe pulse following dye injection for a right femoral arteriogram. *1*, Before dye. *2*, One minute after dye. *3*, Fifty seconds after procaine. *4*, Five minutes after procaine.



A. *B.*

Fig. 7.—Large toe and thumb pulses recorded (*A*) before and (*B*) after popliteal embolectomy.

Fig. 8 shows toe pulses recorded during a femoral arteriogram. Relatively normal left toe pulses are present in the upper record, and "saw-toothed" right toe pulses are seen in the bottom record. These recordings were made during an arteriogram in which 10 c.c. of 1 per cent procaine was injected into the right femoral artery before injection of the dye. The right pulse doubled in amplitude 45 seconds after the procaine was injected. The left toe pulse did not increase in size. Fifteen seconds after 20 c.c. of 35 per cent Hypaque was injected into the right femoral artery, the right toe pulse practically disappeared. It returned to its original amplitude approximately one minute after the dye injection was completed.

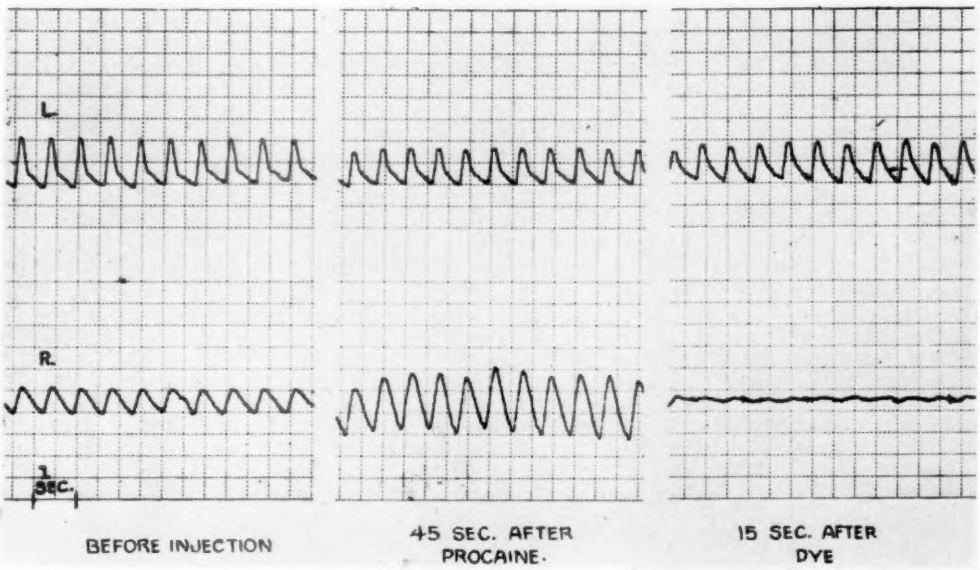


Fig. 8.—Large toe pulses recorded during femoral arteriogram. The right toe pulse is grossly abnormal in form. Injection of procaine into the right superficial femoral artery was followed by increase in right toe pulse amplitude, and injection of dye was followed by a gross decrease in amplitude. Left toe pulse changed little.

Fig. 9 shows an unusual reaction, apparently related to allergy. It is a record of the left and right large toe pulses made during an attempted right femoral arteriogram. The patient had a palpable right femoral pulse. When procaine was injected intradermally and subcutaneously prior to insertion of the arteriogram needle through the skin, the pulse in the right toe disappeared and that in the left toe diminished in amplitude. The arterial puncture attempt was unsuccessful, presumably because of spasm of the artery, and the arteriogram was postponed. Inflammation and edema then developed in the groin and upper thigh where the procaine had been placed. Subsequently, an intradermal skin test with procaine in the forearm demonstrated that the patient had a true allergy to this substance. The arteriogram was later successfully performed using Xylocaine as the local anesthetic.

Fig. 10 shows left and right toe pulses made the day following insertion of a right superficial femoral bypass homograft in a 53-year-old man with

diabetes. The maximum temperature recorded in the right toes during a vasodilatation test, carried out at 20° C. prior to operation was 25° C. After operation the maximum temperature increased to 31.5° C. The right and left large toe pulses recorded postoperatively are of normal amplitude. However,

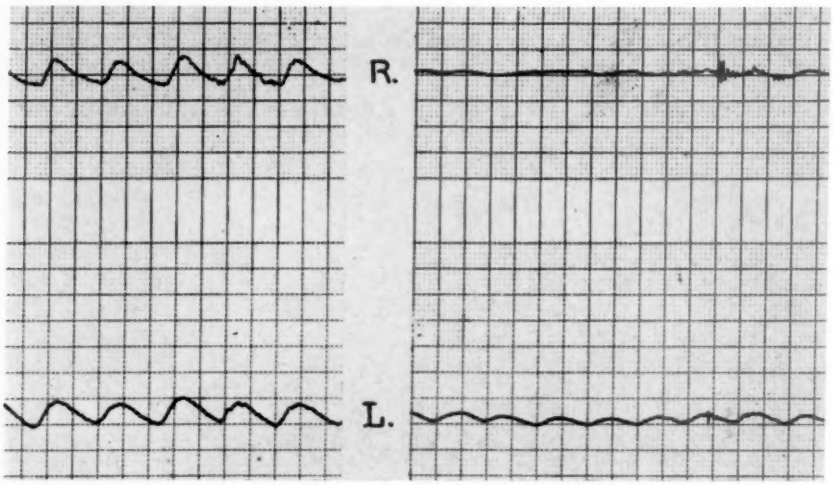


Fig. 9.—Right and left large toe pulses recorded during a femoral arteriogram. The right toe pulse practically disappeared and the left diminished in size when procaine was injected intradermally for local anesthesia. The patient subsequently was shown to be allergic to procaine.

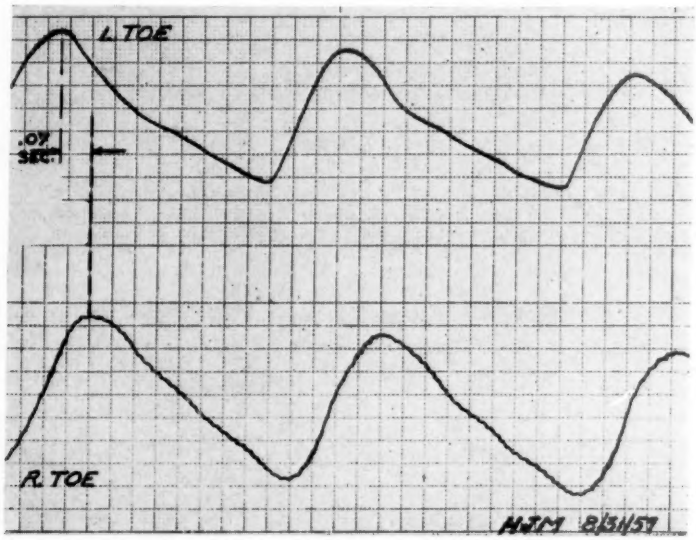


Fig. 10.—Left and right toe pulses one day after insertion of a right superficial femoral bypass homograft, in a 53-year-old diabetic man. Note delay in right toe pulse onset and peak. The patient regained palpable right popliteal, dorsalis pedis, and posterior tibial pulses and had a good clinical result.

the onset of the pulse on the right is delayed 0.05 seconds compared to the onset in the left toe, and the peak is further delayed. This record illustrates that adequate flow may be present when an abnormal pulse wave form and a delay in transmission of the pulse are present.

SUMMARY AND CONCLUSIONS

Digital pulse amplitude, contour, and timing may be easily recorded by means of a simple externally applied transducer and may provide useful information when rapid changes in limb circulation occur. Digital pulses in the opposite limb may be recorded simultaneously as a control.

Arteriospasm frequently occurs during arteriography and occasionally may be of sufficient intensity to obliterate the digital pulse.

The digital pulse wave may return to normal in amplitude and contour following insertion of an autogenous vein graft or following endarterectomy. However, the failure to return to normal does not preclude a good clinical result.

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DISCUSSION

DR. JOHN H. OLWIN (Chicago, Ill.).—I should like to ask two questions: (1) Does the device register changes following reflex heat and (2) does it show changes in the digital pulse following lumbar sympathetic block?

DR. ROBERT S. SHAW (Boston, Mass.).—The estimation of severity of ischemia by some measurement of arterial perfusion pressure in the ischemic tissue is a useful method. We have attempted this by measuring arterial pressure at various levels down the leg, thigh, calf, and ankle. This is performed using an ordinary blood pressure cuff at the various levels and taking as appropriate blood pressure the cuff pressure which just obliterates the digital plethysmographic pulse. The same thing, of course, could be done by palpating a pedal pulse if one were palpable. This method has been useful in evaluating the relative significance of segmental occlusions where they are multiple, for instance, in iliac and in tibial vessels. It is also useful in locating and evaluating occlusive disease where arteriographic examination is lacking.

DR. ROBERTS (closing).—Such studies have been done. In fact, some of these records show the difference between a warm room and a cold room. In general, this will not greatly change the contour or timing of the pulse. It will greatly change the amplitude and allowances must be made for this fact before reaching any conclusion.

I want to thank Dr. Shaw for his remarks and agree with him that it has been a useful tool to us in evaluating the pressure in the artery at different levels—in just the manner that he mentioned—using a cuff. One can record the distal pulses in the digits and obtain the occlusive pressure required to obliterate them.

A METHOD OF CARDIAC BYPASS WITH AUTOGENOUS OXYGENATION

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INTRACARDIAC surgery carried on with the aid of total cardiac bypass, total body perfusion, and frequently elective cardiac arrest has now found its place in the standard practice of surgery. The successful clinical applications of oxygenators of the bubble, membrane, and disc types have all been adequately documented.[1, 4, 5]

It has seemed apparent to us for some time that total body perfusion with oxygenation by means of the subject's own lungs, that is autogenous oxygenation, should be feasible and, indeed, more desirable than the use of an artificial oxygenator. This paper describes the evolution of such a method and outlines the techniques as it is now employed in the laboratory of experimental surgery in this university.

METHOD OF GROUP ONE EXPERIMENTS

Mongrel dogs of medium weight were employed and an attempt was made to exclude animals with distemper. Intravenous pentobarbital sodium was used as the anesthetic agent. As soon as the initial dose had been administered, an endotracheal tube was inserted and connected to a mechanical respirator supplied with 100 per cent oxygen. The arterial blood pressure was measured via a catheter in the femoral artery connected either to a mercury manometer or to a Statham strain gauge and Sanborn multichannel recorder. The venous pressure was measured either in the inferior or the superior vena cava, or both, by means of a saline manometer or a Statham gauge and Sanborn recorder. A convenient electrocardiographic lead was recorded and monitored in many of the experiments.

Electric heating pads were placed beneath the animal and additional precautions were taken against cooling in an attempt to maintain normal body temperature during the perfusion. A bilateral thoracotomy was performed through the fourth intercostal spaces and the sternum was transected. The pericardium was opened widely, the venae cavae were prepared in the standard way for cannulation, and the aorta and pulmonary artery were dissected from each other.

In the initial series of 52 experiments the plan was to bypass the heart without a pump to substitute for the right ventricle and to permit the lungs to carry on their normal function. Thus, although complete bypass was accomplished, the circuit included only one pump which substituted for the left ventricle.

The right heart was bypassed in a passive manner by a Y-shaped cannula system, with limbs in the venae cavae and stem in the main pulmonary artery, into which it was introduced

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through an incision in the outflow tract of the right ventricle. There was no pump and no reservoir in the closed system connecting the venae cavae to the pulmonary artery.

The left atrium was drained by a plastic cannula with its mouth placed in the most dependent portion of the chamber and its distal end suspended in a graduated open reservoir 12 inches below the operating table.[7] Drainage was found to be most satisfactory if the tube was brought out through a separate stab wound in the chest wall at a level lower than the left atrium. The blood was pumped from the reservoir by a Sigmamotor or other pump (vide infra) via a bubble trap into a systemic artery. Early in the series the internal mammary artery was employed because of its location within the operative field, but because of the technical difficulties encountered on occasion, and the unsuitability of this vessel for use in clinical practice, the femoral artery was used in later experiments. In many of the experiments a rotameter flow meter[8] was placed in the system, and in all experiments provision was made to measure the flow rate directly.

Bypass was generally begun by opening the drain from the left atrium and starting the pump to the systemic artery. The pump rate was adjusted to give a systemic blood pressure of approximately 90 mm. Hg. Shortly thereafter the venae cavae and pulmonary artery were compressed against the indwelling cannulae by means of ligatures. Following this the ascending aorta was clamped and cardiac arrest was produced by the Melrose technique.[6] In a few experiments the right side bypass was completed and allowed to function before the left bypass was begun.

The course of the circulation when bypass was complete was from the left atrium to the dependent reservoir from whence it was pumped via the flow meter and bubble trap into the aorta distal to its occluded ascending portion. Blood from the systemic veins flowed through the cannulae in the venae cavae and into the lungs without a special pump. The pressure in the venae cavae was sufficient to cause blood to flow through the low resistance pulmonary vasculature. In the majority of dogs the right ventricle was opened and a ventricular septal defect was made and repaired.

At the conclusion of the intracardiac procedure and before the ventriculotomy was completely closed, the clamp was removed from the ascending aorta. The first blood that perfused the coronaries was allowed to escape and, after forceful cardiac contractions had resumed, closure of the right ventricle was completed. Postoperative care included the standard measures of pleural space drainage, replacement of blood loss, maintenance of normal body temperature, and administration of antibiotics.

RESULTS AND DISCUSSION OF GROUP ONE EXPERIMENTS

Fifty-two experiments were performed in the manner outlined and 31 animals survived. Analysis by the method of Van Slyke and Neill of arterial samples drawn during perfusion showed that saturation with oxygen was complete. Venous samples had low oxygen saturation when the rate of perfusion was relatively low, but they were in the normal range when the flow rate approximated 100 c.c. per kilogram of body weight per minute. Metabolic acidosis of a severe degree developed frequently following perfusion.

This poor survival rate caused us to experiment with tubing of different sizes for the shunt from the venae cavae to the pulmonary artery, pumps with high amplitude and low amplitude pulsations, varying flow rate up to 100 c.c. per kilogram of body weight per minute and a combination of perfusion with hypothermia. None of these measures altered the survival rate and, therefore, we were obliged to re-examine our basic concept of perfusion with autogenous oxygenation employing a simple pump on the left side of the circuit and no pump on the right side. It was self-evident that blood flowed through the bypass of the

right heart because of the pressure gradient between venae cavae and pulmonary artery. It was apparent that elevated venous pressures were needed to overcome the resistance in the pulmonary vascular bed pertaining in the conditions of the experiment. With narrow tubes connecting the venae cavae to the pulmonary artery, venous pressure was frequently 40 cm. saline, and with the wider tubing a satisfactory flow resulted when the venous pressure was 30 cm. saline. The elevation of venous pressure was produced by induction of marked hypervolemia at the beginning of perfusion. As much as 50 to 75 per cent of the dog's estimated blood volume was transfused before a flow rate of 100 c.c. per kilogram of body weight per minute could be achieved. At the end of perfusion it was necessary promptly to correct the hypervolemia in order to prevent cardiac failure and pulmonary edema. Hypotension developed frequently in the early postperfusion period. This usually required an infusion of l-norepinephrine and may have resulted from pooling of relatively large amounts of blood in the venous bed. If problems of this type were frequent in animals without cardiac disease and with normal pulmonary arterial pressure (measured in several instances) what could be expected if this system of perfusion were applied to patients with high pulmonary vascular resistance? This experience forced us to abandon our original concept based for the most part on the experimental work of Starr, Jeffers, and Meade.[9] We concluded that total body perfusion with autogenous oxygenation would be practical only if two pumps were employed, one between the left atrium and the femoral artery and the other between the venae cavae and the pulmonary artery.

Before proceeding with the use of this type of system we carried out a short series of experiments in which the right heart alone was bypassed. The cavae were cannulated and connected by a closed system via a Sigmamotor pump to the pulmonary artery. We were able to maintain normal blood pressure and low venous pressure with high perfusion rate (up to 120 c.c. per kilogram of body weight per minute). Faster flow rates tended to result in frankly negative pressure in the proximal superior and inferior cavae and systemic hypertension. In most experiments with very high flow rates flutter of the caval walls resulted in some irregularity of flow as well as local injury to the vessel. We, therefore, adopted the technique of draining the venae cavae into a dependent open reservoir and pumping from this chamber into the pulmonary artery. We found this method infinitely more satisfactory than applying suction directly to the venae cavae in a closed system. This is in agreement with the findings of others.[2]

We had previously been satisfied that bypass of the left heart could be achieved by draining the left atrium into an open reservoir and pumping the blood from there into the femoral artery. The next step was to investigate the possibility of performing total cardiac bypass with a combination of the techniques that had been developed for the right and left sides individually. The original method used in the first 52 experiments was modified, therefore, to include an open reservoir for collection of systemic venous flow and a pump to force this blood into the pulmonary vasculature.

METHOD OF GROUP TWO EXPERIMENTS

Eighteen dogs were employed. The details of preparation were exactly the same as in the previous group, except that the hemoglobin, blood urea nitrogen, serum electrolytes, and transaminase were determined preoperatively.

Samples of arterial blood for determination of pH* were obtained immediately following cannulation of the femoral vessels. Further samples were obtained during thoracotomy and perfusion and at intervals of 30 minutes for the first 4 postoperative hours. The venae

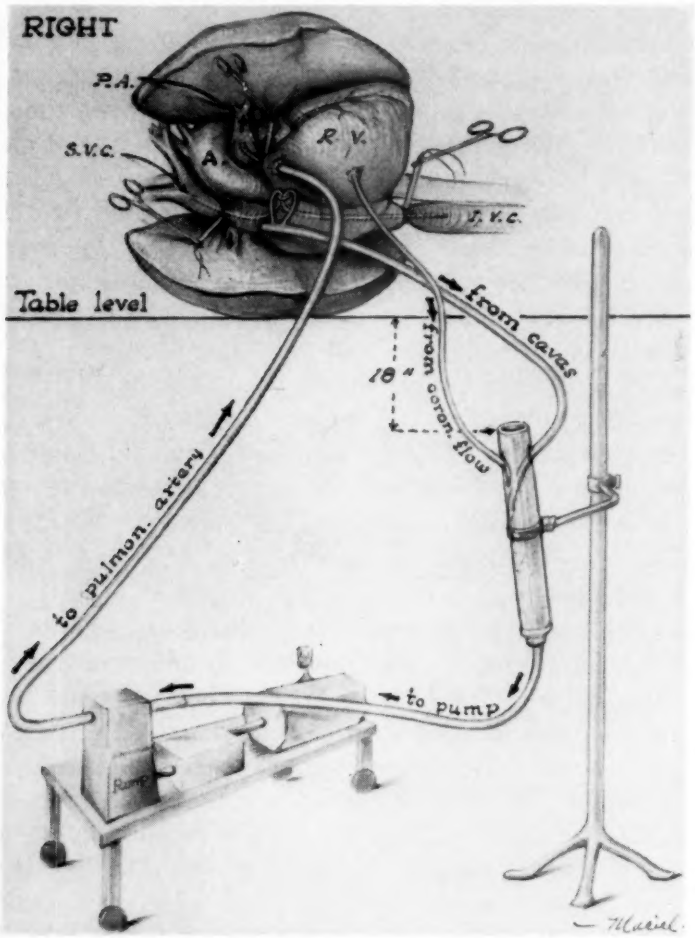

Fig. 1.—Right side bypass. Systemic and coronary venous blood is collected in an open reservoir. It is pumped from there into the pulmonary artery through a cannula inserted near the pulmonary valve or in a branch in the left upper lobe.

cavae were cannulated in the standard manner and were drained by a common tube into an open reservoir placed 12 inches below the right side of the operating table. The blood was pumped from the reservoir by a Sigmamotor system using a gum rubber segment (⅝ inch i.d.) in the pump box and Tygon tubing (½ inch i.d.) attached to a cannula in the pulmonary artery. In later experiments pulmonary artery cannulation was accomplished through a medium-sized branch in the left upper lobe rather than the outflow tract of the right ventricles.

*pH measurements were performed anaerobically on whole blood with a model G Beckman pH meter.

Fig. 1 illustrates the cannulations, the relative position of the reservoir, and the course of the blood through the right side bypass.

The left atrium was cannulated with Tygon tubing (¼ inch i.d.) and drained into an open reservoir placed 12 inches below the left side of the operating table. The blood was pumped from this reservoir by a second pumping unit of the same type. However, between the pump and the femoral artery there were a rotameter flow meter and a special filter and bubble trap.

Fig. 2 shows the drain from the left atrium to open reservoir. The location of the flow meter and combined filter and bubble trap is given with relation to the pump and the systemic arterial system.

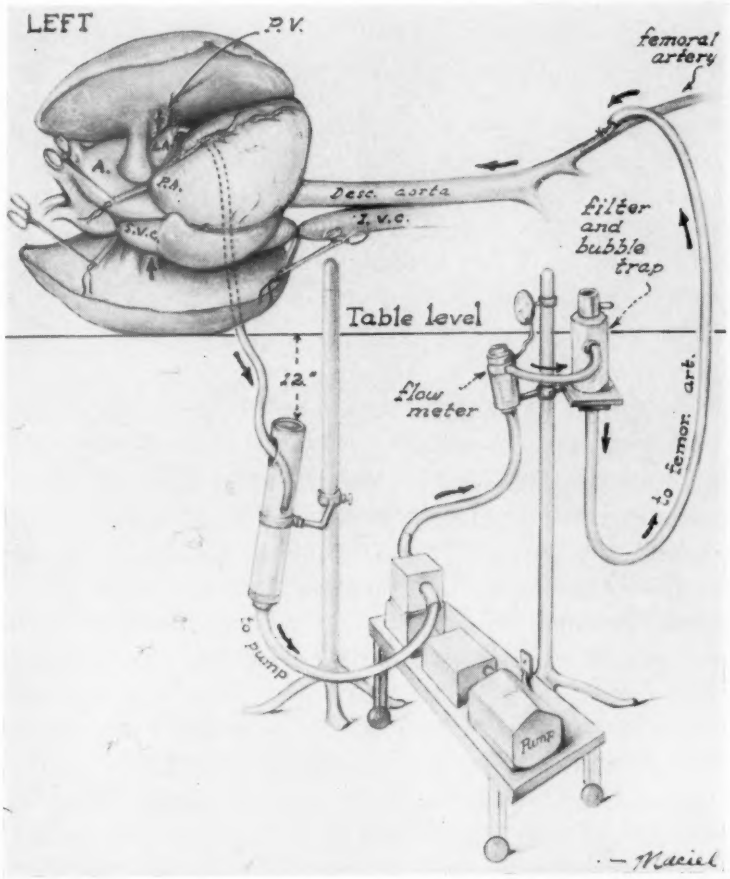

Fig. 2.—Left side bypass. The left atrium is drained into an open reservoir. The course of the blood is shown through the flow meter, filter-bubble trap, and into the femoral artery.

When cannulation was complete, partial right side bypass was begun by opening the drain from the venae cavae to the right reservoir and starting the pump on that side. A screw clamp on the venous drainage line was adjusted to give the fastest flow rate possible without lowering the pressure in the inferior cava. A stab wound was made into the right ventricle and Tygon tubing (¼ inch i.d.) introduced to drain the coronary venous blood since the Melrose technique was not employed in this group and there was perfusion of the coronary circuit. This tube led into the right reservoir along with the one for caval drainage. The venae cavae then were closed around their cannulae and the pulmonary artery around its cannula or at the valve level in those experiments employing cannulation of a peripheral

branch of the artery. During this time the Sigmamotor pump was regulated to keep the volume of blood in the right reservoir more or less constant. Small transfusions, 50 to 100 c.c., were given if necessary to maintain normal systemic pressure. As soon as a "steady state" was achieved, the drain from the left atrium was opened and the left pump was started. Total cardiac bypass continued for 30 minutes, after which the animal was excannulated and the chest was closed. The same postoperative care was given that was described for group one experiments.

One additional measure was employed during perfusion and often for several hours afterward that had not been used in the first group of experiments. This was the administration of sodium bicarbonate solution intravenously (4.4 mEq. per kilogram of body weight diluted in 500 c.c. of 5 per cent glucose in water). This was suggested by the acidosis which complicated earlier experiments; Ito[3] has described a similar experience and his plan of treatment was adopted.

RESULTS OF GROUP TWO EXPERIMENTS

Eighteen dogs were perfused by this technique. Of these, two died and were considered failures and three had to be discarded from the series due to circumstances which made it impossible to evaluate them (severe pneumonia, postoperative pneumothorax due to displaced pleural drain, and dislocated arterial cannula with shock due to blood loss in the postoperative period). This gave a survival rate of 13 of 15 which was much better than could be obtained with the various modifications of technique employed for experiments in Group One.

Regulation of the two separate pumps proved less difficult than was anticipated. Experience soon demonstrated that transfusion was required at a rate of approximately 1 c.c. per kilogram of body weight per minute of total cardiac bypass and this we believe served to replace blood lost in the wound. The systemic pressure was maintained at or about 110 mm. Hg and the venous pressure practically unchanged from preperfusion levels. The mean rate of perfusion varied between 85 and 95 c.c. per kilogram of body weight per minute mean values and the standard deviations for arterial pressure and perfusion rate are given in Table I. When the flow rate was less than desired the drain from the venae cavae was opened further and the right pump speeded —a maneuver that always permitted speeding the left pump. If the caval drain was already fully open, the right pump was accelerated so as to give a transfusion of 100 c.c. from the reservoir. If hypovolemia was the reason for the low flow rate, transfusion always permitted acceleration of the pumps. It was somewhat surprising at first to see that the volume transfused from the

TABLE I

	FLOW RATE (C.C./KG. BODY WEIGHT/MIN.)		MEAN ARTERIAL PRESSURE DURING PERFUSION		MEAN pH		
	LOWER LIMIT	UPPER LIMIT	LOWER LIMIT	UPPER LIMIT	BEFORE PERFUSION	DURING PERFUSION	LATE
	85	96	109 mm. Hg	141 mm. Hg	7.54	7.44	7.45
std. dev.	−25	+26	−23	+16	±0.07	±0.09	±0.04

The mean flow rates and arterial pressures during perfusion are given along with the standard deviation from the lower and upper limits. The mean values for pH include determinations made up to 3 hours after perfusion ("Late" column).

right reservoir promptly collected in the left reservoir. Thus it was possible to increase the flow rate by transfusing from the right side reservoir and maintaining a constant volume in the one on the left side.

Arterial samples drawn within a short time after the animals were anesthetized usually had a pH that was normal or somewhat alkalotic. However, there was a tendency for acidosis to develop while thoracotomy and cannulations were being completed. This could be corrected and recently it has been prevented by manual compression of the bag attached to the endotracheal system and hyperventilation of the lungs. The administration of sodium bicarbonate intravenously also corrected the abnormal pH, and associated with its use we noted that the arterial pressure was maintained at a higher level on the average. The mean values for pH of arterial samples are given also in Table I. The low pH that complicated many of the experiments requires further study since the metabolic factor may be of major importance and most of our efforts have been directed toward improved elimination of carbon dioxide.

In 5 dogs the pulmonary artery pressure was measured through a cannula inserted into a branch of the artery to the right upper lobe. The pressures were normal before perfusion started and they remained unchanged during the period of cardiac bypass. This proved that use of a pump between venae cavae and pulmonary artery that was identical with the pump employed between left atrium and femoral artery did not cause abnormal variations in pressure in the pulmonary vascular bed. It seemed safe to conclude that it was not necessary to employ pumps with different characteristics on the right and left sides, in an attempt to duplicate the characteristics of the normal ventricles.

DISCUSSION

Use of the lung for oxygenation during cardiac bypass appears to hold several advantages over use of an artificial oxygenator. Careful regulation of the inflation of the lung in this perfusion technique results in full oxygenation and elimination of carbon dioxide with a simpler extracorporeal apparatus and system of controls than is required for most artificial lungs. The hazard of gas embolism, inherent to some degree in all oxygenators employing the bubbling principle, is definitely reduced. The use of this more physiologic method completely avoids many problems associated with mechanical lungs which employ artificial membranes between the blood and oxygen. Moreover, this method would have special advantage in clinical conditions associated with increased flow through the bronchial arteries. The flow from the bronchial vessels into the left atrium would drain with the stream from the pulmonary veins. No special provisions would be required for this additional volume in the left atrium and engorgement of the pulmonary vasculature would be entirely prevented. Finally, the apparatus employed for this type of bypass is easily sterilized and assembled and its operation does not require a team of experts.

Use of two open reservoirs as employed in this extracorporeal circuit has several advantages. They serve as simple bubble traps and this is particularly

important on the left side of the circuit where air may be carried with the blood from the left atrium after the right side of the heart has been opened. Draining the cavae and left atrium into open reservoirs by gravity prevents excessive suction which may lead to flutter or collapse of the vessels near the ends of the inlying tubes. Of equal or greater importance is the fact that with a separate reservoir in each side of the circuit, precise balancing of the output of the two pumps is not essential. We quickly found that if the pumps were pumping at different rates, the one going faster transferred blood to the opposite reservoir. Thus the homolateral reservoir lost blood and the contralateral one gained an equal volume. It was a simple matter then to correct this inequality of flow.

There are disadvantages to this method of autogenous oxygenation which should be mentioned. The lungs must be ventilated with special care during the bypass period. The surgeon may find it inconvenient to have them fully inflated and some movement transmitted to the heart. Placement of the tube for drainage of blood from the left atrium requires meticulous care and, in our experience, this part of the extracorporeal circuit is the one most likely to cause difficulty. Cannulation of the pulmonary artery may present problems if this method is used clinically. This cannula and attached plastic tube from the right side pump may be an additional hazard to the surgeon whose field in the heart and at its periphery is overcrowded with instruments and connections to the extracorporeal apparatus.

Surgical residents have been able readily to learn this technique and in association with a cardiologist and two technicians carry out well-controlled experiments in total cardiac bypass. Comparisons between artificial and autogenous oxygenation are of considerable value for the improvement of all methods of total body perfusion. Methods of autogenous oxygenation certainly merit further study because of the variety of clinical applications that appear to exist for them.

SUMMARY

1. Fifty-two experiments were performed in which cardiac bypass was accomplished by autogenous oxygenation and a single pump that substituted for the left ventricle. The results obtained by this system which lacked a pump to act as the right ventricle are summarized and some interpretations are given.

2. Eighteen perfusions were done with autogenous oxygenation and two pumps, one for the pulmonary circuit and the other for the systemic circuit. The survival rate is given along with flow rate, arterial pressure, and the pH of arterial samples. Technical details related to drainage of pulmonary venous blood via the left atrium are given. The use of an open reservoir on each side of the circuit is described and regulation of two independent pumps is outlined.

3. Advantages and disadvantages of perfusion with autogenous oxygenation are reviewed. It is concluded that the technique described will give an excellent survival rate in the laboratory. Clinical application, however, should be delayed at least until control of acid-base balance is improved and further experience is gained through sham operations on the open heart.

We are indebted to Miss Daphne Anderson, Mrs. T. Wieke, and Mrs. Ardeth Byrley for technical assistance. Mr. Adolph Feibel made valuable contributions through suggestions and development of special equipment.

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DISCUSSION

DR. LEWIS H. BOSHER, JR. (Richmond, Va.).—What are the circumstances in the left ventricle under open heart surgery when you are draining the left atrium? Can you work within the left ventricle? How satisfactory is this?

DR. SHABETAI (closing).—When working within the interventricular cavities, we have found that the best technique has been to insert yet another drain into the heart which we place into the apex of the left ventricle. This additional cannulation with a small tube serves two important functions. The first is that it acts as a very efficient mechanism to remove bubbles of air from the left ventricle which must enter into the left ventricle when the right ventricle is opened in the presence of the ventricular septal defect. The left ventricular tube has another function in that it acts as a monitor and safeguard for the drain which is in the left atrium for the bypass; because if this drain ceases to function well, then blood will flow down the left ventricular drain. The presence of blood in this drain is a sign to us that the left atrial drain is not working well. It is also a safeguard because if the left atrial drain does cease to work well at any instant, then the blood will be carried into the left ventricular drain and thence to the reservoir for the left-sided bypass. With these two drains in place, the conditions within the ventricle are excellent for work on ventricular septal defects.

It is also our opinion that one could approach the mitral valve satisfactorily from the right side with this arrangement and that the aortic valve would also be amenable for treatment.

CLINICAL EXPERIENCE WITH A ROTATING DISC OXYGENATOR

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INTRODUCTION

A ROTATING disc oxygenator, modified from devices introduced by Björk[2] and by Kay and Cross,[5] has been employed for heart-lung bypass in 75 surgical cases involving correction of cardiac defects. The search for a satisfactory extracorporeal circulation had led first to a comparison of the relative merits of a bubble oxygenator[7, 10] and a rotating disc oxygenator.[8] Each oxygenator performed successfully in the laboratory. The bubble oxygenator was then used as a part of an extracorporeal circulation for heart-lung bypass in several patients, but the results were not entirely satisfactory.

Because the disc oxygenator had proved especially safe and simple in laboratory trials, it too was subjected to clinical trial. The results were better than those obtained with the bubble oxygenator. It was fully realized that a necessary learning process had been completed with the bubble oxygenator and that some original mistakes were not repeated. The improved results with the rotating disc oxygenator could not therefore be attributed entirely to the differences between the oxygenators.

THE DISC OXYGENATOR

The first disc oxygenator constructed (Fig. 1) consists of 70 stainless steel discs, 0.8 mm. thick and 12.7 cm. in diameter. These are mounted on a central steel shaft, with 5 mm. spacers separating them. The disc assembly is supported horizontally by Lucite end plates within a Lucite cylinder 41 cm. long and 16 cm. in diameter. The discs lie eccentrically in the cylinder so that the lateral walls of the cylinder lie 2.0 cm. from the edges of the discs. This clearance has been found extremely important in preventing turbulence and foaming at high flow rates. The end plates are held in place with screws and are sealed with partially seated rubber rings.

Blood is introduced in the bottom of one end of the cylinder and removed from the other at right angles to the direction of blood flow through the oxygenator. This technique diminishes splashing against the discs at the inlet end. The filmed blood is exposed to a mixture of 98.5 per cent oxygen and 1.5 per cent carbon dioxide, which is introduced through a stainless steel tube running the length of the oxygenator 5 mm. above the discs. The oxygen tube is perforated with many small holes to distribute the gas mixture evenly through the chamber. The gas mixture is introduced into the oxygenator at a rate of 8 L. per minute for most perfusions. The Lucite cylinder has 5 small vents to allow the escape of excess gas. The discs and the Lucite chamber are coated with a thin film of Dow-Corning Antifoam A before use. The coating is best applied by spraying a 1:5

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mixture of Antifoam and ether on the discs and cylinder with a compressed air atomizer. The oxygenator reservoir is heated with several lamps in a standard foot-warming cradle which covers the unit while it is in use.

The oxygenator is primed with 2,000 c.c. of blood which immerses the discs to a depth of 4.0 cm. The exposed area of the 70 discs is 1.09 square meters. At a disc rotation of 100 r.p.m. the exposure is 109 square meters per minute. This area has provided adequate oxygenation. An additional 500 c.c. of blood is required to fill the extracorporeal circulation completely.

At first the oxygenator cylinder and end plates were sterilized with benzalkonium chloride, although the stainless steel discs were autoclaved. Three infections with *Pseudomonas aeruginosa* made a change in sterilizing technique mandatory. Chlorine water in a concentration of 1:100,000 is now employed to sterilize the oxygenator chamber and end plates. No infections have occurred since this method of sterilization was adopted. A 40-disc oxygenator of similar design is employed for small children and infants.

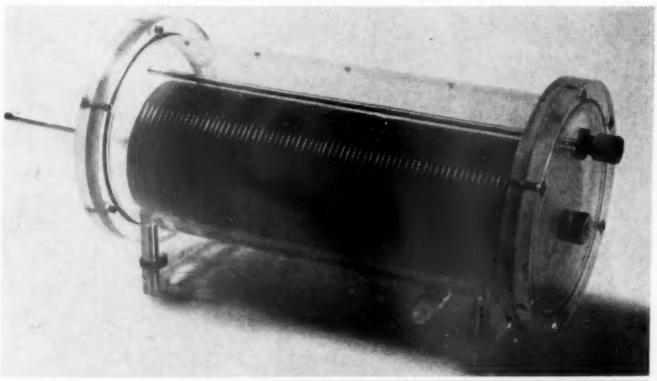

Fig. 1.

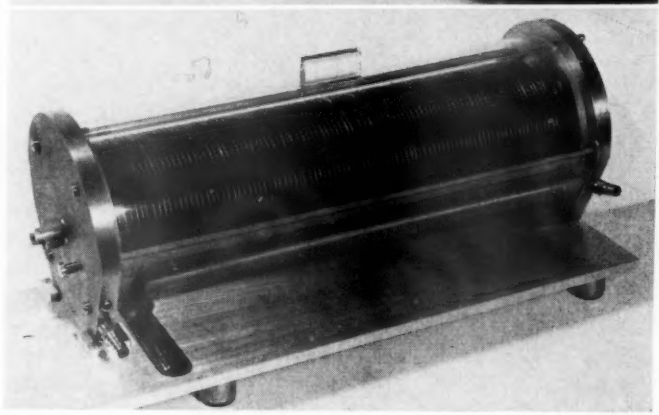

Fig. 2.

Fig. 1.—First disc oxygenator with 70 discs. A smaller 40-disc oxygenator of the same design is used for infants.

Fig. 2.—Present 90-disc unit which can be autoclaved.

At present an oxygenator containing 90 discs 0.4 mm. in thickness and 12.7 cm. in diameter is also being used (Fig. 2). In this unit, which can be completely autoclaved, the discs are placed 4.0 mm. apart. A larger oxygenating surface has been provided. In design, the unit is similar to the original oxygenator, although several modifications have been made. Blood enters the unit through an end plate and is removed through a well in the oxygenator trough. To diminish turbulence along the line where the rotating discs leave the blood, the oxygenator has been widened. Openings are present in each end plate to allow sampling and temperature recording. The priming volume of the oxygenator is 2,500 c.c. blood.

TECHNIQUE OF PERFUSION

The extracorporeal circulation is made up of the rotating disc oxygenator and a Sigmamotor pump, model T65 or TM1. Blood is pumped directly from the venae cavae to the oxygenator. Arterial perfusion is accomplished by cannulating the femoral artery below the profunda branch. Blood from the open heart is returned by suction to a reservoir where it is allowed to flow over plastic sponges coated with Antifoam to remove bubbles. It is delivered into the extracorporeal circulation by means of the venous pumping head when the line connecting the reservoir to the extracorporeal circulation is opened intermittently. Stainless steel connectors with locking nuts (Fig. 3) provide maximum safety in assembling the components of the extracorporeal circulation. These connectors are employed throughout the extracorporeal circuit.

A bubble trap between the oxygenator and the arterial pumping head is believed to be a necessary safety device. At flow rates approaching 3,000 c.c. per minute turbulence may be present in the oxygenator and small bubbles may be carried beneath the surface of the blood by the rotating discs. These bubbles occasionally escape into the arterial line and are recovered from the bubble trap at the end of the perfusion. The priming blood is filtered, but no filter is present in the circuit. When the oxygenator is primed the discs are rotated slowly to prevent drying of the blood film. The blood is exposed to air alone to prevent the removal of carbon dioxide and a marked rise in pH. The flow of oxygen over the discs is begun only at the start of the perfusion. The blood is circulated a few times to remove bubbles through the extracorporeal circuit before perfusion.

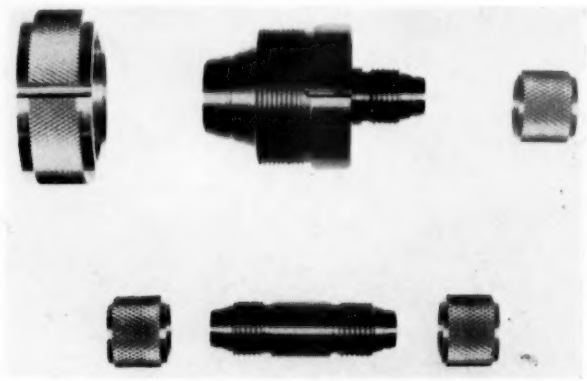

Fig. 3.—Connectors for the rubber ventricles and connecting lines.

A perfusion rate of 70 to 80 c.c. per kilogram per minute is attempted for most patients. This flow rate is increased to 100 c.c. per kilogram per minute for children with tetralogy of Fallot, but in adults the flow rates are lower. These rates lie slightly below the optimal rates suggested by Clark[3] (Fig. 4). At the start of perfusion the clamps are removed from the vena cava cannulae an instant after arterial flow has begun. The amount of blood in the patient is thus increased initially, with resulting improved venous return.[4] Obstruction of venous return is avoided by placing the venous cannulae only a short distance into the superior and inferior venae cavae. Chattering of the caval catheters from too rapid removal of venous blood is infrequent and has occurred only in infants. The heart-lung bypass is run in parallel with the patient's own circulation for a short period before total bypass is begun. Balance in the extracorporeal circuit is easy to achieve in most patients, and the venous return is sufficient to allow perfusion at the proposed rate of arterial flow.

At the end of heart-lung bypass the extracorporeal circulation is again run in parallel with the patient's circulation for a short time. Great care is taken to restore the blood in the extracorporeal circulation to its original volume before the bypass is completed. Blood loss is measured by weighing sponges and by measuring blood aspirated

from the chest. The amount of blood introduced into the extracorporeal circulation is measured carefully and the amount remaining at the end of perfusion is again measured. These, with the volume of blood administered intravenously, allow an immediate estimate of the patient's blood loss and replacement. This method of determining blood loss and replacement has proved satisfactory; the patients are not weighed after the operation.

Before instituting heart-lung bypass, 1.5 mg. of heparin per kilogram of body weight is given to the patient intravenously. This drug is neutralized after perfusion with 1.5 mg. protamine for each milligram of heparin injected.

The patient's condition during heart-lung bypass is followed by continuous recording of electroencephalographic and electrocardiographic patterns, as well as the pressure in the femoral artery and the inferior vena cava. The measurement of central venous pressure is a sensitive index of the state of the perfusion and correlates very closely with the volume of blood in the oxygenator. During heart-lung bypass the arterial pressure is maintained in most patients between 60 and 100 mm. Hg. At the start of the perfusion the arterial pressure may be 10 to 20 mm. Hg lower than the pressure which is reached a few minutes after complete bypass is established. Vasopressor agents have been administered only rarely to increase the pressure during perfusion.

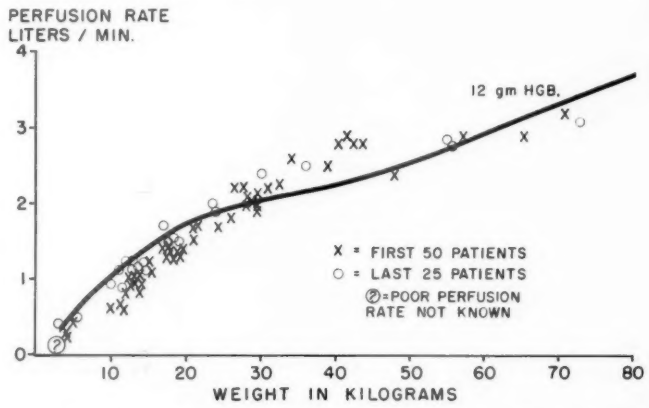

Fig. 4.—Flow rates achieved have been compared with optimum perfusion rates recommended by Clark.[3]

The time of heart-lung bypass has varied from 15 to 60 minutes. In most cases, correction of the cardiac defect is accomplished with a bypass of less than 30 minutes. During heart-lung bypass the rectal temperature drops 1° to 3° C. The temperature drop has been partially controlled by warming the oxygenator and by placing the patient on a mattress which is filled with warm water before heart-lung bypass is begun.

The average rate of hemolysis in the arterial line of the extracorporeal circulation at the end of perfusion is 75 mg. per cent. This amount of hemolysis is a reflection of the attempt to reach optimum flow rates[1] with equipment which produces significant hemolysis at high-volume flow rates. The average arterial oxygen saturation at the beginning of perfusion is 96 per cent, and this falls during perfusion to 92 per cent. There is an average increase of 27 to 33 per cent in arterial-venous difference during perfusion.

Cardiac arrest has been produced in 12 cases with a solution containing potassium citrate and magnesium sulfate.[9, 12] Its use is reserved for those cases in which careful placement of a large Ivalon patch is necessary to close a ventricular septal defect and it has been limited to 30 minutes' duration. Intermittent aortic occlusion for repeated periods of 4 minutes provides a bloodless field for direct closure of most ventricular septal defects. Neither cardiac arrest nor aortic occlusion is necessary for repair of atrial septal defects and pulmonic stenosis.

The patients are maintained on light general anesthesia throughout the operation. Five minutes before heart-lung bypass d-tubocurarine is injected intravenously in a dose

of 0.5 mg. per kilogram. The patients frequently recover some consciousness during perfusion. If additional muscle relaxant is necessary, one-half the original dose is injected into the extracorporeal circulation. Following heart-lung bypass the patients are again maintained on light anesthesia and are fully awake at the end of the operation.

ACID-BASE BALANCE

In 51 patients, the pH, HCO_3, and pCO_2 values in arterial and venous blood were determined (1) before heart-lung bypass, (2) at the start of complete bypass, (3) at the end of complete bypass, (4) one-half hour after bypass, and (5) 2 to 5 hours after the operation. It was possible in 17 of the 51 patients to obtain arterial or venous samples for acid-base study the day before and the day after the operation. A typical example of these studies can be seen in Table I.

TABLE I. VENTRICULAR DEFECT
(F. L., 4 W. M., #729545, MARCH 11, 1958)

	pH	HCO_3	pCO_2	LACTIC ACID (mEq./L.)	OXYGEN SATURATION (%)
Before operation	7.41 (V)	27.8	45	—	—
Before perfusion	7.54	14.0	17	7.4	97
Start of bypass	7.49	15.3	21	7.0	99
End of bypass	7.44	14.8	23	7.2	99
½-hour after perfusion	7.55	12.6	15	7.7	100
5 hours after perfusion	7.29	22.0	47	1.9	96
First posterative day	7.36 (V)	25.7	47	—	—

A uniform pattern of acid-base change has been found in these studies. The patients were alkalotic as a result of hyperventilation by the anesthetist before the bypass. At the start of heart-lung bypass the pH fell toward normal, but the patients continued to be alkalotic. The average pH change from the beginning to the end of perfusion was 0.04. One-half hour after perfusion the patients were again alkalotic.

After operation the patients developed a combined respiratory and metabolic acidosis. The average pH of these patients was 7.29; HCO_3, 20.9; and pCO_2, 45. The following day the values had returned to normal. These changes are outlined in Fig. 5. Determinations of lactic acid in arterial blood were made during and after operation in 16 patients. The lactic acid values remained within normal limits; in most of the patients the values were decreased during the time acidosis was present.

In all cases, the surgical procedure was carried out through a bilateral anterior intercostal incision with division of the sternum. Limitation of respiratory excursion resulted from the surgical incision, and it is believed that this contributed to the acid-base changes noted. Acid-base studies carried out after thoracic operations in which an extracorporeal circulation was not employed showed similar but less marked changes.

Electrolyte studies were made in 17 cases. No significant changes in the values of sodium, potassium, or chlorides were found during or after operation.

The day following operation a slight drop in chlorides was noted. In the 5 cases in which calcium determinations were made, no changes in calcium levels were noted during and after operation.

POSTOPERATIVE PROBLEMS

The patients have been awake at the end of operation. The electroencephalograms have given no evidence of hypoxia or cerebral damage during heart-lung bypass. Two patients experienced mild hallucinations during the first 12 hours after the operation, but were normal the following day.

The major problem in the care of these patients has been control of pulmonary secretions. Diligent attention to voluntary coughing by the patient and the liberal use of endotracheal suction have been of great help in clearing retained secretions. At times neither physical examination nor a chest film has been a good index of retained secretions. The patients have had fewer pulmonary secretions when the fluid intake has been limited to 40 to 50 c.c. per kilogram per day during the first 48 hours following operation.[11] Tracheotomy was carried out in 11 patients, mostly infants for whom it was hoped that better control of secretions and the use of a positive pressure respirator would aid in recovery. Several of the tracheotomies were done early in the series. Tracheotomies have not been necessary recently except in infants.

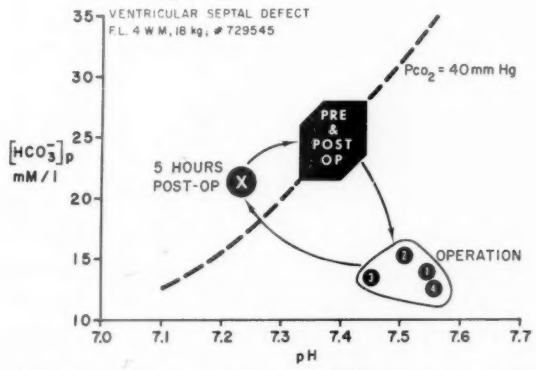

Fig. 5.—Acid-base changes occurring in patients undergoing heart-lung bypass. (*1*) Before perfusion. (*2*) start of perfusion, (*3*) end of perfusion, and (*4*) one-half hour after perfusion. Adapted from Davenport.[6]

Bleeding after operation has not been troublesome. One patient required reoperation for postoperative bleeding following aortic valvulotomy. The total drainage of blood and serum during the 18 hours after the operation while the tubes are in place has varied from 200 to 500 c.c. for most of the patients. Cardiac operations performed on these patients at an earlier time have not resulted in a large additional blood loss during or after bypass.

A severe transfusion reaction with temporary renal shutdown occurred in one patient. A mild hemolytic reaction was noted in a second patient; a third was later readmitted to the hospital with jaundice which was believed due to serum hepatitis. The first urine specimen following operation contained hemoglobin in at least three other patients, but the specimens were negative thereafter.

Complete heart block occurred in two patients following operation but was relieved by sublingual Isuprel in doses of 2.5 mg. and reversion to normal sinus rhythm occurred finally. Varying degrees of dissociation have been noted for short periods in a few patients following operation but the dissociation has reverted to normal sinus rhythm in a few hours.

Pulmonary hypertension has been a serious problem. The patients with pulmonary hypertension have had increased tracheobronchial secretions which have been difficult to evacuate, particularly in the smaller patients. In addition, right-heart failure has occurred in these patients, and they have required digitalis and diuretics in the postoperative period. Pulmonary hypertension has been present in many of the patients who died after the operation.

Upon completion of heart-lung bypass, the femoral artery cannula has been removed and the artery repaired by direct suture with 5-0 silk, except in several infants, where the artery has been ligated. Pulses have been palpable in the leg following operation and there has been no evidence of arterial insufficiency. However, on return visits following discharge a few patients have not had palpable pulses in the leg, although the legs have been warm and the patients asymptomatic. One adult returned 3 weeks after discharge, with acute thrombosis of the femoral artery at the suture line. Reanastomosis was carried out and circulation in the limb was then satisfactory.

Early in our experience, infection occurred in 3 young patients after the operation. In each case the infection was due to *Pseudomonas aeruginosa* and was the result of improper sterilization of the oxygenator with benzalkonium chloride. The organisms recovered from the blood stream were insensitive to the many antimicrobial agents administered. Two of the patients, each of whom had undergone repair of a ventricular septal defect, developed at long last an abscess in the left anterior chest wall. The abscesses were drained and the ventriculotomy sutures were found lying free in the abscess cavity. The wounds healed and the children have remained well. There was no evidence of infection of the sutures used to close the ventricular septal defect in either patient. The third patient had a large atrioventricular canal closed with a compressed Ivalon patch. The blood stream could not be sterilized. The patient died in heart failure that was due in part to the overzealous administration of intravenous fluids. At postmortem examination the Ivalon patch contained no gross vegetations but Pseudomonas organisms were recovered from it.

RESULTS

Seventy-five patients have undergone correction of cardiac defects with the aid of an extracorporeal circulation utilizing a rotating disc oxygenator (Table II). Two infant patients were operated upon with the intent of employing heart-lung bypass, but in one the difficulties in arterial cannulation made a transventricular valvulotomy for pulmonary stenosis advisable, and, in the second case, bleeding encountered from the inferior vena cava during dissection in an obliterated pericardial space forced postponement of the

operation. The majority of the patients have been children between 10 and 30 Kg. in weight. Seven patients weighed more than 30 Kg.; the heaviest was an adult weighing 72.7 Kg. Six infants weighed less than 10 Kg. each.

TABLE II. 75 DISC OXYGENATOR PERFUSIONS

	PATIENTS	DEATHS
Ventricular septal defect	27	4
Atrial septal defect	21	1
Pulmonic stenosis	10	0
Tetralogy of Fallot	4	1
Aortic stenosis	6	2
Aortic window	2	1
Atrioventricular canal	2	2
Mitral insufficiency	1	0
Miscellaneous	2	2

Ventricular Septal Defect.—In 27 patients a ventricular septal defect was repaired. An Ivalon patch was necessary for adequate closure of the defect in 5 patients. In the remaining 22 patients, closure of the ventricular septal defect was accomplished with horizontal mattress sutures of 3-0 silk. Three patients had in addition atrial septal defects which were also repaired. Mild stenosis of the pulmonary valve was present in two patients and was corrected. One patient with corrected transposition of the great vessels was approached through the functioning left ventricle and, following closure of the ventricular septal defect, the stenotic mitral valve was dilated. In one patient who had recovered from bacterial endocarditis, the ventricular septal defect was associated with a sinus of Valsalva aneurysm. These lesions were closed by direct suture. In only one patient were multiple ventricular septal defects recognized. Successful repair of a ventricular septal defect was accomplished in two infants weighing 4.3 and 5.0 Kg. The use of tracheotomy and of mechanical ventilation was believed to be of help in the recovery of these infants.

TABLE III. DEATHS IN 75 PERFUSIONS

ANOMALY	AGE, SEX, RACE	CAUSE OF DEATH
Ventricular defect	2 mos. WF	Pulmonary hypertension, respiratory insufficiency
Ventricular defect	3 mos. WM	Pulmonary hypertension, respiratory insufficiency
Ventricular defect	2 WM	Pulmonary hypertension
Ventricular defect	10 WM	Aortic insufficiency, technical errors
Atrial defect	52 WF	Pulmonary hypertension, right-to-left shunt
Atrioventricular canal	5 WF	Infection
Atrioventricular canal	3 WM	Mitral insufficiency, reoperation
Aortic stenosis	14 WF	Acute aortic insufficiency
Aortic stenosis	28 WM	Ventricular fibrillation
Tetralogy of Fallot	7 WF	Technical error
Aortic window	3 WF	Pulmonary hypertension
Atrial, ventricular, and venous abnormalities	3 mos. NF	Correction impossible
Transposition	11 mos. WM	Correction impossible

Pulmonary hypertension, with pulmonary artery pressures greater than 80 mm. Hg systolic, was present in 7 patients, 2 of whom were infants with associated atrial septal defects. Three of the four patients who died following repair of a ventricular septal defect had such pulmonary hypertension (Table III).

Atrial Septal Defect.—Atrial septal defects of the secundum type were repaired in 21 patients by direct suture with interrupted figure-of-eight mattress sutures of 3-0 silk. The single death in this group occurred in an adult patient with pulmonary hypertension and a right-to-left shunt through the atrial defect. Preliminary palpation of the atrium with a finger before heart-lung bypass frequently failed to disclose the extent or multiplicity of the defects present. Two patients were found to have large fenestrated defects, and in 3 patients there were multiple atrial defects. Pulmonary valve stenosis and anomalous pulmonary venous drainage from the right lung were present as associated lesions in two patients. Pulmonary valve stenosis was present as an additional anomaly in one patient. These associated anomalies were all corrected.

Pulmonic Stenosis.—Pulmonary valve stenosis was corrected in 9 patients and isolated infundibular stenosis in one patient without a mortality. In 3 of the patients, atrial septal defects were present as associated but minor anomalies, and were corrected. An attempt was made in each case of pulmonary valve stenosis to reconstruct a tricuspid pulmonary valve by division of the stenosed valve along its commissures. The pulmonary valve was exposed through a vertical incision in the pulmonary artery. In none of the patients was there an unrecognized ventricular septal defect or infundibular stenosis.

Other Lesions.—Correction of tetralogy of Fallot was accomplished in 5 patients. The ventricular septal defect was closed with a compressed patch of Ivalon. The outflow tract of the right ventricle was enlarged by removing portions of the infundibular stenosis and by inserting a diamond-shaped patch of compressed Ivalon as a gusset in the wall of the right ventricle. The single death among these patients was the result of inadequate closure of the ventricular septal defect. Following restoration of the circulation the patient developed a large left-to-right shunt with severe pulmonary edema.

An attempt was made to correct aortic stenosis in 6 patients. The aortic valve was approached through the aorta, which was cross-clamped. Cardiac arrest was not produced, and the interruption of coronary circulation was limited to 5 minutes. The stenosis was valvular in 4 patients and subvalvular in 2 patients. The surviving patients were improved but the results were less satisfactory than the results following correction of pulmonary valve stenosis. In one patient death was the result of acute aortic insufficiency following rupture of an aortic valve cusp during attempts to dilate a subvalvular stenosis. The second death was the result of persistent ventricular fibrillation which occurred while correction was being carried out.

The remaining lesions were complicated, and many of the patients were infants. The mortality rate was high (Table III) in this group. Most disappointing were the deaths of 2 patients with atrioventricular canal. One of the children died from infection with *Pseudomonas aeruginosa.* The second patient developed severe mitral insufficiency following operation and died when a second attempt was made later to repair the mitral valve.

The majority of the deaths in the entire group of 75 patients occurred (1) in cases of infants with complicated lesions, (2) in patients with pulmonary hypertension, and (3) in cases in which technical errors were made during operation. The deaths were not related directly to the heart-lung bypass, although the perfusion in infants was often very difficult and could not be excluded as a cause of death.

SUMMARY

Seventy-five cases of cardiac defects were treated by surgical operations during which a safe, easily controlled extracorporeal circulation with a rotating disc oxygenator was employed for heart-lung bypass. The patients were maintained on heart-lung bypass in satisfactory condition for as long as an hour. There were minimal changes in acid-base balance during perfusion. The patients all developed a mild combined respiratory and metabolic acidosis immediately after the operation, but the acid-base values returned to normal the next day. No significant electrolyte changes were noted.

Thirteen deaths occurred in this series, including 4 among 27 patients with ventricular septal defects and 1 of 21 patients with atrial septal defects. There were no deaths among 10 patients with pulmonic stenosis.

ADDENDUM

Since this paper has been presented the total number of patients undergoing heart-lung bypass with the extracorporeal circulation described has increased to 122. The cases include 43 patients with ventricular septal defects of whom 6 did not survive operation, 33 patients with atrial septal defects of whom only one died, 20 patients with pulmonic stenosis without a mortality, and 9 patients with tetralogy of Fallot of whom 3 died. The autoclavable stainless steel disc oxygenator in several sizes is being employed routinely. Perfusion rates have been increased to 2,300 ml. per square meter of body surface per minute. The use of the vertical sternum-splitting incision has been found to improve ventilation following operation and to reduce postoperative pulmonary complications.

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COMPLICATIONS PECULIAR TO OPEN HEART SURGERY

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INTRODUCTION

THE advent of practical pump-oxygenators opened new vistas in cardiac surgery. The initial enthusiasm of those who first applied these devices in clinical surgery was quickly tempered as the difficulties of total body perfusion became apparent. As was anticipated all the problems attendant to other forms of thoracic surgery were encountered. However, new problems arose, particularly in the immediate postoperative period. Unexplained and unexpected deaths within the first few days after operation occurred with appalling frequency. Mortality rates of 40 to 60 per cent were not uncommon in the dark days of 1955 and 1956, as new surgical teams entered the venture. Perplexed surgeons, cardiologists, and pathologists brooded over the "sudden death syndrome" that was seen in patients whose initial response was promising.

It is remarkable how quickly the picture has brightened since that time. This is attested to by the steady decline in over-all mortality figures. Better understanding of the problems attendant to body perfusion has been one factor of improvement. Improved surgical techniques may also play an important part. Functional cardiac anatomy is very perplexing, and what looks like a satisfactory repair to the neophyte may not stand the test of time.

A detailed enumeration of the complications encountered in open heart surgery that utilizes the pump-oxygenator would serve little purpose. Such a list would be a lengthy reduplication of facts well known to every well-grounded and experienced surgeon. However, attention may well be directed to those problems that are peculiar to operations where total body perfusion is employed. At the risk of oversimplification, we have grouped these problems under four headings. Each of these four major complications can be anticipated, often prevented.

METABOLIC ACIDOSIS

The occurrence of metabolic acidosis following total body perfusion was recognized early in the development of open heart surgery. It was suggested that acid base imbalance reflected damage to the blood itself by the pump-oxygenator. The aura of mystery that shrouded metabolic acidosis has been dispelled by better understanding of its cause, signs, and prevention.

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Metabolic acidosis is the product of low perfusion, whether by inadequate flow from the pump-oxygenator or reduced cardiac output. Since the early clinical efforts with pump-oxygenators followed the "azygous flow principle,"[2, 3] acidosis of varying degree was a certainty in almost every operation. Reproduction of this phenomenon in the laboratory is readily accomplished by the simple expedient of reducing the caval return to the heart by partial occlusion (Fig. 1).[4] It is now apparent that open operations performed at normal temperature under low flow are tantamount to operations performed during chronic shock. Metabolic acidosis will surely follow; its degree will be dependent upon the duration and the inadequacy of the perfusion.

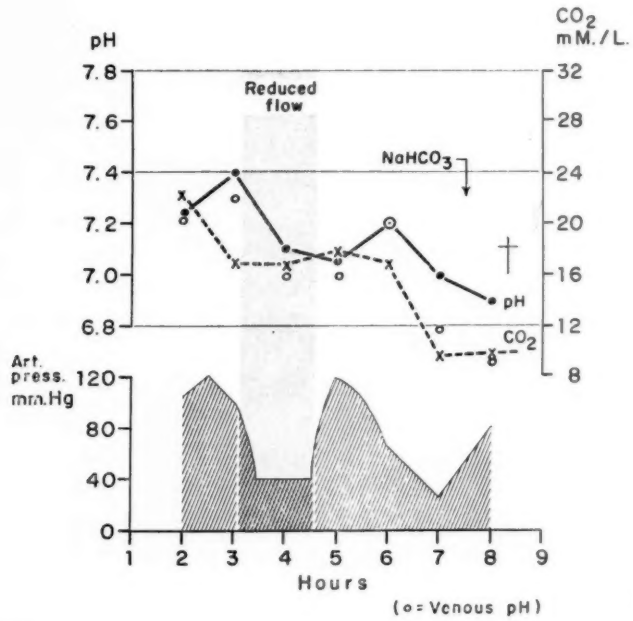

Fig. 1.—Chart showing the course in a dog in which partial ligation of the venae cavae reduced the arterial pressure to 40 mm. Hg. Fall in pH of the arterial blood (black dots and solid line) parallels the more severe fall in central venous pH (white dots). Note the progressive decrease in CO_2 content, expressed in millimols per liter, until $NaHCO_3$ was administered. (Miller, Edward: Cleveland Clin. Quart. 24: 195, 1957.)

Clinical recognition of metabolic acidosis is not difficult. It should be anticipated whenever hypotension is present during the procedure—whether this occurs during, before, or after the perfusion is not important. Since the venous pH does not fall immediately after the operation, the surgeon should not be misled; it has been our observation that the significant drop in pH occurs approximately 3 hours after surgery or perhaps later. The patient with significant acidosis has a poor color, low blood pressure, lethargy, and rapid pulse. The alert nurse and resident staff will frequently describe the patient as "too quiet." It appears that the younger patient is more susceptible and tolerates acidosis less than does the adult. Death from metabolic acidosis is associated with respiratory failure as the pH and the Co_2 values fall to critical levels.

Prevention of metabolic acidosis depends upon a high-flow perfusion that is preceded and followed by adequate cardiac output. For this reason, we insist upon a continuous monitor of the mean arterial pressure throughout the entire procedure. Blood samples are taken before, during, and after the perfusion and the blood pH determined. Particular care is taken to see that these determinations are repeated 3 hours after surgery and again at the sixth hour. If a low pH is expected, it is standard procedure to restore acid base balance as accurately as possible by giving soda bicarbonate by slow intravenous drip.[4, 7] Sodium bicarbonate (4.5 mEq. per kilogram of body weight), commercially available as 50 c.c. ampuls containing 44.6 mEq., is diluted with a double volume of 5 per cent fructose in water and started as a slow intravenous drip to be injected during the first 6 hours following operation. In the majority of operations we are able to prevent or control a dangerous degree of metabolic acidosis; nevertheless, it is still a factor when longer perfusions are needed for very small children, particularly those in the cyanotic group.

OVEROXYGENATION

Data on the toxicity of oxygen is scarce; however, a wide range of observations in animals and man suggest that continuous exposure in high concentration may be responsible for protoplasmic changes in the central nervous system, lungs, heart, liver, and kidney.[12, 13] If a human is exposed to high oxygen tension, manifestations of oxygen toxicity will occur with symptoms of vertigo, nausea, confusion, irregular respirations, and finally convulsions with loss of consciousness.

With the many improvements made upon pump-oxygenators, the probability arises that under certain conditions such a device may be too efficient. This possibility was suggested by Kirklin and his associates.[6] It cannot be overlooked that direct contact between the blood and raw oxygen without an intervening membrane does not simulate normal physiology. Variations in the solubility of oxygen in blood with changes in temperature may be quite significant when there is marked discrepancy between the temperature of the machine and the patient.

It is our belief that overoxygenation of blood is a distinct possibility and that it is most likely to occur under the following conditions[5]: (1) during recirculation of the blood through the oxygenator prior to perfusion, (2) during perfusion of a small patient with an oxygenator of large capacity, and (3) during partial cardiac bypass with a low flow rate.

We have found the Clark Polarograph* to be extremely useful for regulating oxygen tension and have incorporated its use as standard procedure in the operating room. While the blood is being recirculated through the oxygenator prior to perfusion, an air-CO_2 mixture is used instead of pure oxygen. The polarographic reading obtained from this air-oxygenated blood is used as a base line. During cardiac bypass that base line is maintained by adding oxygen and by adjusting the speed of rotating discs (Kay-Cross oxygenator).

*Made by Yellow Springs Instrument Company, Inc., Yellow Springs, Ohio.

Although it is difficult to prove, excessive oxygenation of blood by the heart-lung machine may have been responsible for sudden death in the postoperative phase, particularly in small patients. It appears that the polarograph measuring oxygen tension provides a better estimate of high oxygen values than does measurement of oxygen content or oxygen saturation. Careful attention to this phase of over-all body perfusion has been paralleled by consistent improvement in clinical results.

COMPLETE HEART BLOCK

Interruption of the conduction system during open heart surgery may be a fatal complication. Whereas complete heart block may be a transient problem, it is mandatory that an effective ventricular rate be maintained until spontaneous conversion to sinus rhythm occurs. A pacemaker which utilizes intrapericardial electrodes has been very helpful in supporting patients with complete A-V dissociation through the critical postoperative period.[1, 10]

If our concept of the conduction pathways is correct, it is remarkable that certain septal defects are ever corrected without producing complete block. High interventricular defects associated with dextroposition of the aorta, atrial septal defects of the ostium primum type, or complete absence of the atrial septum seem to be the lesions whose correction may produce heart block. Elective cardiac arrest is often followed by heart block during the first few minutes after re-establishment of coronary flow. Poor perfusion of the myocardium with associated surgical trauma may also be a factor in producing heart block. This was observed in our earlier experience where low-flow perfusion was employed or faulty cannulation resulted in very poor coronary perfusion. In several of these cases complete block occurred even though anatomic disruption of the conduction bundle seemed unlikely.

When closure of a surgical defect produces heart block the question will immediately arise as to whether or not a suture improperly placed is the responsible factor. The surgeon must then decide on the advisability of reopening the closed defect and trying again in the hope that removal of the offending suture will promote return to sinus rhythm. At present it is our growing conviction that this is not the procedure of choice. On numerous occasions we have seen heart block revert to sinus rhythm spontaneously within minutes or hours or even days after onset; on the other hand, there have been two occasions where a sinus rhythm has been lost hours after the operation to be replaced by total heart block. It is our present policy that any patient with an unsatisfactory rhythm following open cardiotomy should be protected by inserting intrapericardial electrodes and having a pacemaker available, if not actually in use.

At present we are using a compact homemade pacemaker.[10] This instrument uses relatively low voltage when internal electrodes are applied directly to the heart muscle. It has been our practice to apply both electrodes to the myocardium and to test the instrument before the patient is taken off the pump-oxygenator run. As a rule, the pacemaker is used in children whose ventricular rates are below 90 and in adults whose rates are below 80 (Fig. 2). On two occasions conversion of atrioventricular block to a sinus rhythm occurred while

the child's heart rate was maintained on the pacemaker on the third and thirteenth days, respectively, after surgery. Whether or not the pacemaker in itself influences a change in rhythm or whether reversion is spontaneous is impossible to state at this time. Regardless of this, the supportive action of the properly used pacemaker may be lifesaving and should be included in the armamentarium of every surgical group performing cardiac surgery.

LEFT HEART DISTENTION

A wide variety of potential pulmonary complications exist in open heart surgery. Severe pulmonary hypertension, improper use of fluids, pulmonary air emboli, poor anesthetic technique, and inadequate tracheal toilet will account for most. These were anticipated and are usually avoidable. It is now apparent that serious, even fatal, pulmonary problems occur secondary to left heart distention during partial or total bypass, particularly if elective cardiac arrest has been employed.

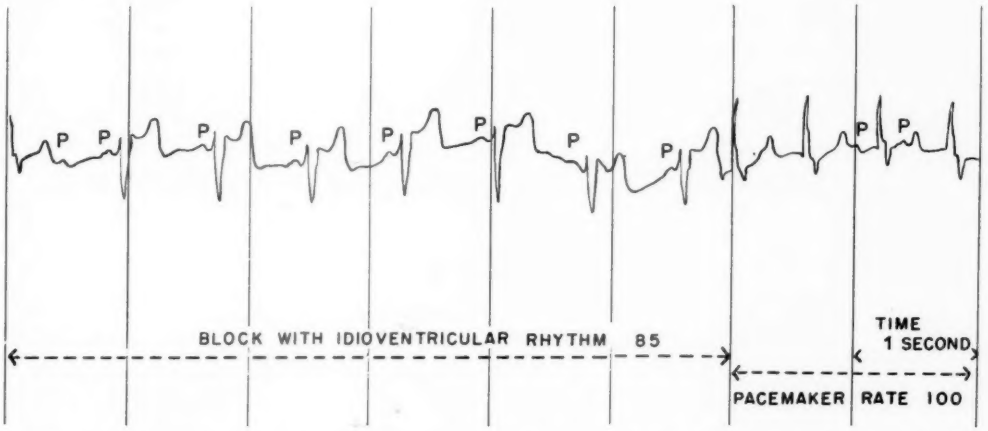

Fig. 2.—Reproduction of electrocardiographic tracing of a 2-year-old boy with tetralogy of Fallot. Complete atrioventricular block was evident after termination of cardiac arrest. Half of the P waves fall in the ventricular complexes, whereas the others precede them. Although the ventricular rate was 85, the pacemaker was connected and a rate of 100 was forced upon the ventricles. The high sharp peaks are from the pacemaker current. They initiate ventricular complexes of totally different shapes from those of the previously seen idioventricular QRS complexes.

We were slow to recognize the import of left heart distention even though this complication and its fatal sequelae were clearly demonstrated on too many occasions. It is now clear that significant damage produced by left heart distention will be reflected in the left ventricular myocardium and in the pulmonary vascular bed.[8] The significance of such damage will be directly proportional to the severity of the changes that occur in either locale.

Myocardial Damage Following Left Heart Distention.—On the basis of clinical and experimental observations it is quite obvious that the heart is intolerant of sudden and violent distention. Whether this is produced by overloading or partial paralysis is of secondary importance. The overloaded heart may show a rapid decrease in efficiency manifested by arrhythmia, falling cardiac output, and loss of an effective beat. In a recent report Littlefield and associates[11] described the histopathologic changes that occur in the left ventricular myocardium which has been permitted to overdistend during recovery from elective

cardiac arrest. From a practical standpoint those surgeons who have tried to convert the distended heart in ventricular fibrillation know that it is almost impossible to do so until the ventricle has been partially decompresed. Overdistention of the left ventricle may be a disastrous complication. Its prevention is mandatory.

Overloading of the Pulmonary Vascular Bed Secondary to Left Heart Distention.—Thoracic surgeons have long recognized that mechanical occlusion of a major pulmonary vein may result in diffuse interstitial hemorrhage with destruction of the involved parenchyma. The normal lung tolerates poorly sudden pressure elevations in the pulmonary venous bed. If the pressure within the left atrium is suddenly elevated to a pathologic level (for example to 45 or 60 cm. H_2O), this pressure will be reflected in a retrograde fashion throughout the pulmonary venous circuit into the pulmonary capillaries and irreversible pulmonary damage may ensue. The sequence of overloading of the pulmonary circulation secondary to left heart distention may be seen in open heart surgery that utilizes total body perfusion in different ways.

Forward overfilling of the pulmonary vascular bed: This may occur during partial bypass with sudden overloading of the circulation before caval ligatures are secured. It may also occur during total bypass when the venae cavae are occluded and the right heart is closed, if "extravagant" coronary blood flow occurs. This will rarely lead to pulmonary damage unless pulmonary outflow is impeded.

Filling of the pulmonary vascular bed through collateral vessels: The presence of a patent ductus arteriosus or significant collateral circulation (for example, tetralogy of Fallot) will provoke an abnormal return to the left heart during extracorporeal bypass. This high flow may be seen as it spills through the septal defect during the open cardiotomy; however, as the defect is closed the pressure within the left heart chamber will show an ominous rise. This is of particular significance when elective cardiac arrest has been employed.

Retrograde overfilling of the pulmonary vascular bed caused by impeded venous return: Such overfilling may follow mechanical obstruction of pulmonary veins, obstruction of the mitral valve, or serious mitral valve regurgitation.

Retrograde overfilling by backflow: This is seen in cases where there is significant aortic insufficiency. The retrograde aortic stream from the artificial heart machine will load the left ventricular chamber by way of the incompetent aortic valve.

Retrograde overfilling by dynamic obstruction (Fig. 3): If elective cardiac arrest has been employed the right ventricle may recover more quickly than the left ventricle and a transient period of left ventricular failure may occur. It may also follow when air is present in the coronary arteries. It is seen when ventricular fibrillation occurs during perfusion or when cardiac arrest persists for any reason. Regardless of the cause, the left atrial pressure will reflect a sharp rise to a dangerous level.

That overloading of the left heart with its immediate reflection upon the pulmonary vascular bed and the ventricular myocardium should have been

anticipated is now too clear. The pathologic changes attendant to this serious complication are now recognized and have been reproduced in the experimental laboratory.[9] From a clinical standpoint this complication was most commonly associated with the more complex forms of cardiac disease subjected to open heart surgery and where elective cardiac arrest was needed.

Prevention of left heart distention and its attendant complications may be accomplished easily by the use of a left atrial cannula.[8] In addition to the routine use of the two caval cannulae, we use a third venous cannula inserted into the left atrium from the right side. The point of insertion is usually in the right superior pulmonary vein as it enters the left atrium. A simple purse-string suture will secure the cannula after it has been inserted through a small stab wound. Such a cannula may be placed through the left atrial appendix, but this is not always accessible even when a bilateral thoracotomy incision has been made. Since more of our operations are being performed with a single right thoracotomy, we prefer the right approach to the left atrium.

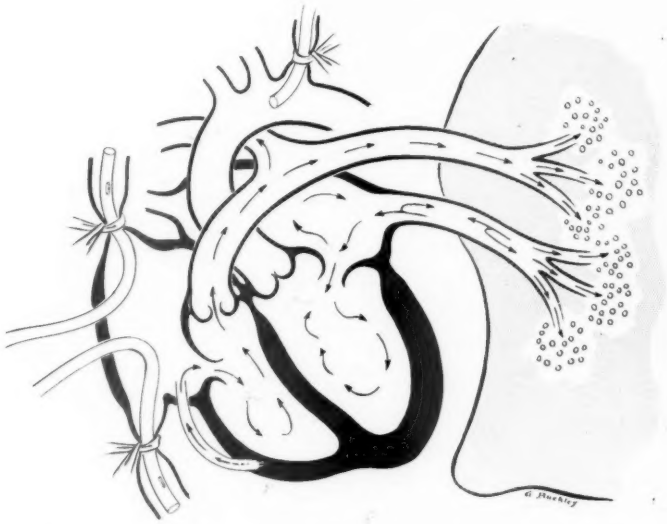

Fig. 3.—Retrograde overfilling of the pulmonary vascular bed occurs because dynamic obstruction due to ventricular fibrillation or inefficient left ventricular beat causes blood from the coronary circulation or from elsewhere to pool in the left ventricle and finally to back up into the pulmonary veins.

This left heart cannula serves two useful purposes: (a) it can afford a constant monitor of the left atrial pressure, and (b) it offers a simple method of venting the left heart into the venous reservoir, affording excellent prophylaxis against left heart distention. The left heart cannula may be used to remove trapped air following closure of the cardiotomy incision during operations upon septal defects or the mitral valve. A provision for aspiration through it is therefore made. Negative pressure should not be applied to the left side cannula before all communication of the left heart cavities with the atmosphere are hermetically closed off lest air be sucked into them. The advantages of left heart cannulation will become apparent with its use, and we consider it a very significant adjunct to the present methods of accepted cardiac bypass when a pump-oxygenator is employed.

CONCLUSION

It would be impertinent to suggest that all complications of open heart surgery are understood or even recognized. Nevertheless, progress has been made, albeit at the price of many bitter disappointments. It is unfortunate that too many teams, starting in too many places, are duplicating the same mistakes. In this field of surgery, successful outcome within the operating room itself does not insure ultimate success. Most deaths following open heart surgery occur in the recovery unit; however, the initiating cause of death will be traced back to the surgical theater. More experience in the labyrinth of intracardiac lesions, recognition of complications peculiar to open heart surgery, better understanding of their etiologies, and more attention to the disasters rather than the triumphs of this spectacular endeavor will lead to better and safer heart surgery.

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DISCUSSION

DR. DENIS G. MELROSE (San Francisco, Calif.).—You have made a point which just cannot be too often emphasized. If you are going to stop hearts, by whatever method you like, you must take appropriate steps to prevent overstretching. It has become a rule

at Stanford to look very carefully at the size of the heart just prior to and just after the heart-lung machine has taken over the circulation. We can be confident that if the heart is reasonably reduced in size after the venous return has been diverted we are not going to have any real difficulties in the stopping or starting of the heart. If the heart does not shrink visibly then we are aware of the dangers. I hope that we may be able to use this technique of venting the left atrium, for I imagine it is a very real asset. I know that hearts will always start again provided they are not overstretched.

DR. JOHN H. GIBBON, JR. (Philadelphia, Pa.).—I was pleased to hear not only our President but others state that adequate blood flows through extracorporeal circuits are important in order to avoid metabolic acidosis. I completely agree with Dr. Effler that if you have an adequate blood flow you are less liable to get metabolic acidosis, although it does occur, as Drs. Effler and Sloan both stated, in other major operative procedures. In our experience it has not been greater than with other major operations. I think, as Dr. Sloan stated, that in the postoperative period the acidosis which occurs for the first 6 hours or so is a combination of respiratory and metabolic—metabolic, if you have an inadequate flow and respiratory because the lungs function poorly. Dr. Effler pointed out one of the reasons for poor pulmonary function in the postoperative period, which is left heart distention.

I have not heard anyone mention whether or not the lungs are currently being ventilated when the heart is bypassed. Four or five years ago we reported, in discussion at the Surgical Forum, some experiments which we had done in the laboratory with a double lumen tracheobronchial catheter separately measuring the oxygen uptake of each lung, occluding the pulmonary artery of one lung for one hour, and then again measuring the oxygen uptake of each lung. The lung whose pulmonary artery had been occluded, showed a decreased oxygen uptake during the first 2 or 3 hours. Since then Kirklin and his group, our group, and others have not ventilated the lungs. But this is a new and important point about postoperative respiratory acidosis which may result, as Dr. Effler told us, from a so-called blast injury.

Since Pendido, Swan, and Kirklin's paper on excessive oxygenation in a study of bubble oxygenators, most investigators have been rather careful with other types of oxygenators. During the preoperative circulation of donor blood through the extracorporeal circuit before connecting with the patient, we now use air instead of oxygen. Dr. Effler's discussion of this was very interesting.

Nobody has mentioned yet the safe duration of elective cardiac arrest. It is a fascinating field and we do not even know what happens to the temperature of the heart with prolonged arrest and no coronary flow. Dr. Templeton of our Department has maintained elective cardiac arrest for an hour and 40 minutes with recovery of the patient. Last week he corrected a complete transposition of the great vessels with cardiac arrest for 2 hours and 40 minutes. There were good cardiac contractions originally but then a complete left bundle branch block occurred with a ventricular rate of well under 50. The stimulating electrodes that Dr. Effler mentioned were then used. Despite all efforts, however, the child died. It is of some interest that, after 2 hours and 40 minutes of cardiac arrest with potassium citrate, the heart will start and contract well. At autopsy one suture was found which was, I believe, responsible for the complete left bundle branch block.

DR. CHARLES K. KIRBY (Philadelphia, Pa.).—We have encountered two problems which seemed difficult to overcome, and I wonder if Dr. Effler will comment about them. In one instance there was massive flow of perfused arterial blood back through the aortic valve, which was grossly incompetent, but the aortic insufficiency had been masked and not considered significant preoperatively. Soon after opening the left atrium, we were removing 4 L. of arterial blood per minute through the intracardiac sucker, and the total arterial perfusion rate into the femoral artery was about 5 L. per minute. It was necessary to cross-clamp the aorta to stop the free flow from the arterial catheter through the aortic valve and out the left atrium.

We have also encountered the opposite problem, that is such a completely competent aortic valve that no blood came back into the left ventricle. Under these circumstances,

all the blood from the left ventricle was pumped into the left atrium by a few heartbeats and air was then sucked into the left ventricular cavity. This increases the risk of air embolism, and also the regurgitant column of blood is not present as a guide in placing the right number of sutures to correct the insufficiency. Distortion of the aortic valve manually has caused adequate left ventricular filling from above, but this is not a common problem, in our experience, and the left ventricle may empty itself before the need for inducing aortic regurgitation by this maneuver is recognized.

DR. ROBERT J. SCHRAMEL (New Orleans, La.).—We have been interested in trying to determine whether the observed respiratory difficulties following cardiopulmonary bypass are due solely to the chest wall injury, and we have measured the carbon monoxide diffusing capacity rather than ventilatory factors alone. (Slide.)

These studies were carried out in conjunction with Dr. Cameron of our Department of Medicine. Normal values for this procedure vary from 10 to 30 c.c. of carbon monoxide per minute per mm. Hg pressure difference so that preoperation determinations are necessary on each patient. As can be seen from this slide, there is a pronounced depression of the carbon monoxide diffusing capacity in every case. Of equal interest is the observation that diffusion capacity does not return to preoperative levels until 3 weeks after operation. Only 4 patients have been studied by this method. Each of them had a different cardiac lesion. The results observed only suggest that cardiopulmonary bypass per se is associated with pulmonary parenchymal damage. Fortunately this method can be readily adapted to the experimental animal and each of the important variables can be separately evaluated. Our studies in animals have not been completed yet.

DR. FRANK GERBODE (San Francisco, Calif.).—I'd like, if I may, to make a few statements, Dr. Effler, about some of your remarks, all of which I think are extremely pertinent.

First of all, about the safe time for cardiac arrest, we have had many perfusions under arrest up to 45 or 60 minutes, but if we exceed 30 minutes we have noticed the incidence of slow recovery of the heart and the increase of unusual arrhythmias. There is one other way of preventing distention of the left side of the heart, which we employ commonly if the heart is slow in recovering and distention is seemingly imminent or present, and that is to keep the patient on partial bypass. Very often we will pull the tubes back into the atrium and take blood away from the right side, knowing that, of course, what gets into the left side must start on the right side. Therefore, if you take it away from the right side for a longer time, and maintain partial perfusion, some distention can be prevented.

One other slight difference that I would like to mention is about inflation of the lungs. We all paid a great deal of attention to Dr. Gibbon's very nice work about keeping the lungs inflated during bypass. We very soon found that, under the very light form of anesthesia which our anesthetists have been accustomed to employ in the last 4 or 5 years, there is a sedative effect of intermittent partial inflation of the lungs; and if the patient is on very light anesthesia and one stops inflating the lungs, even though they are not contributing anything in the circulation, the patient will wake up. This curiously keeps the patient asleep but still what you might say awake.

DR. EFFLER (closing).—I would like to make several additional comments—Dr. Gibbon mentioned ventilation during total bypass. It is our policy, as mentioned by Dr. Gerbode, to keep the lungs moderately inflated during bypass, but we use room air instead of pure oxygen at this time. The anesthetist declares himself at the onset of total perfusion and switches over from pure oxygen to room air. Whether this practice is justifiable or whether we are simply fanning a bogey, I do not know. Nevertheless this is our present policy.

The possible time limit of elective cardiac arrest is of great interest to us. The longest term of uninterrupted elective cardiac arrest that we have employed is 58 minutes. The heart restarted promptly and this 55-year-old man made a splendid recovery. I do not believe that cardioplegia or total asystole with potassium citrate has a known time limit.

I do believe, however, that the operation which requires unusual periods of total perfusion is particularly subject to metabolic acidosis, temperature changes, and other unpleasant factors already mentioned by Drs. Gibbon and Gerbode. In our initial experimentation with the Melrose technique in Kolff's laboratory, we would stop dogs' hearts for periods of 3 hours; in almost every case we were able to restart the heart quite well even though our primitive perfusion methods were far from ideal. However, many of those dogs died during the first night after operation. We were very much interested to see whether the elective cardiac arrest was the fatality factor or whether it was the prolonged operation during which time the dog was under "inadequate surgical conditions." Serial biopsies of the heart muscle immediately after cardiac resuscitation showed no significant changes regardless of the length of time of cardiac arrest. However, if the dog died 10 or 12 hours after surgery, there were gross and microscopic findings of myocardial necrosis as these dogs invariably died with severe acidosis.

At present we have not set an arbitrary time limit of elective cardiac arrest; however, I must state that we do not prolong the period of asystole nor the time of total perfusion for any longer period than is necessary to accomplish our specific operative procedure. Although no time is intentionally wasted during the open cardiotomy, we do not, on the other hand, monitor the passing minutes.

Dr. Kirby commented on the possible dangers of overdecompression of the left heart. We have not been impressed that evacuation of the left heart is hazardous as it will refill promptly from the returning coronary circulation when asystole is terminated. Needless to say we try to avoid trapping of air in either the right or left side of the heart for reasons that are obvious to all.

DIAGNOSIS AND SURGICAL TREATMENT OF COMMON ATRIUM (COR TRILOCULARE-BIVENTRICULARE)

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THE advent of open heart surgery has emphasized the wide variations in the anatomy of congenital heart defects. Accurate preoperative and operative evaluation of the anatomic details of cardiac malformations has become important now that complete correction so often is possible. The clinical, physiologic, and pathologic features of atrial septal defects in the usual location, of defects of the common atrioventricular canal type, and of atrial septal defects associated with anomalous pulmonary venous connection are now well known.

The rarest type of defect affecting the atrial septum is complete absence of the septum or common atrium. It shares some clinical and anatomic features with defects of the common atrioventricular canal type, while hemodynamically it resembles the condition of total anomalous pulmonary venous drainage. Misinterpretation of certain clinical features of this condition might lead to a mistaken assumption of inoperability.

The purpose of this paper is to report and comment on the pathologic, clinical, hemodynamic, and surgical aspects of common atrium, as determined from our experiences with 5 patients who have undergone operation.

PATHOLOGIC ANATOMY AND EMBRYOLOGY

Cor triloculare-biventriculare, or the terms "absence of atrial septum" or "common atrium," may be used to denote those hearts in which no atrial septal tissue or virtually none exists but in which the ventricular septum is present. The lowermost boundary of the defect is formed by atrioventricular valvular tissue and, in some cases, by a portion of the ventricular septum.

We have recognized two forms of the defect, the partial and the complete, which are similar in some respects to the two forms of common atrioventricular canal.[13] In fact, the characteristics of the lowermost portion of the defect are closely comparable in the matching degrees of the two conditions. In the partial form of both, the septal leaflet of the mitral valve usually is cleft and the lower edge of the defect is composed of fused valvular tissue; the ventricular septum is intact (Fig 1, *A*). In the complete form of each condition, both the mitral and

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the tricuspid valves are cleft and the lower edge of the defect is made up of ventricular septum which itself is in part deficient (Fig. 2, *A*). Four of our patients exhibited the partial form of the anomaly and one the complete. Three patients had a persistent left superior vena cava.

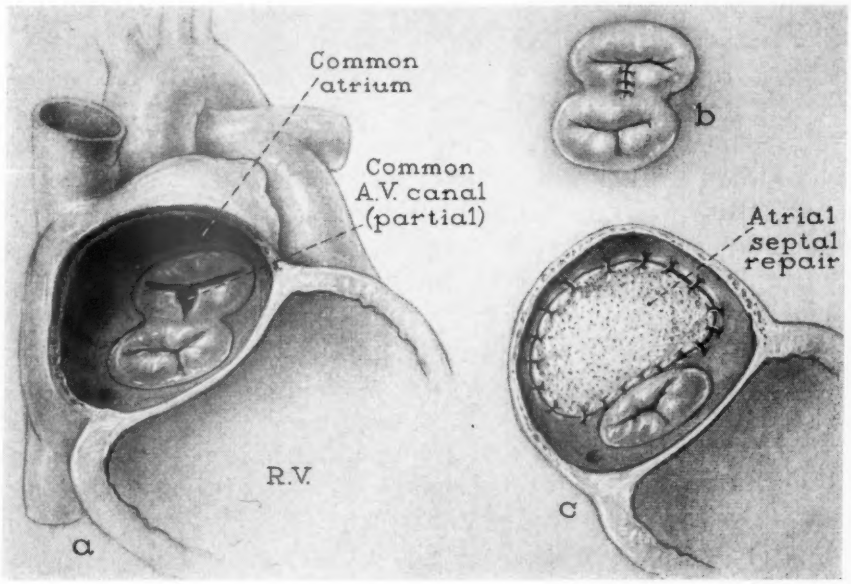

Fig. 1.—Common atrium. *A*, Lower portion of defect, similar to that seen in partial form of common atrioventricular canal. *B*, Suture of mitral cleft. *C*, New atrial septum in place.

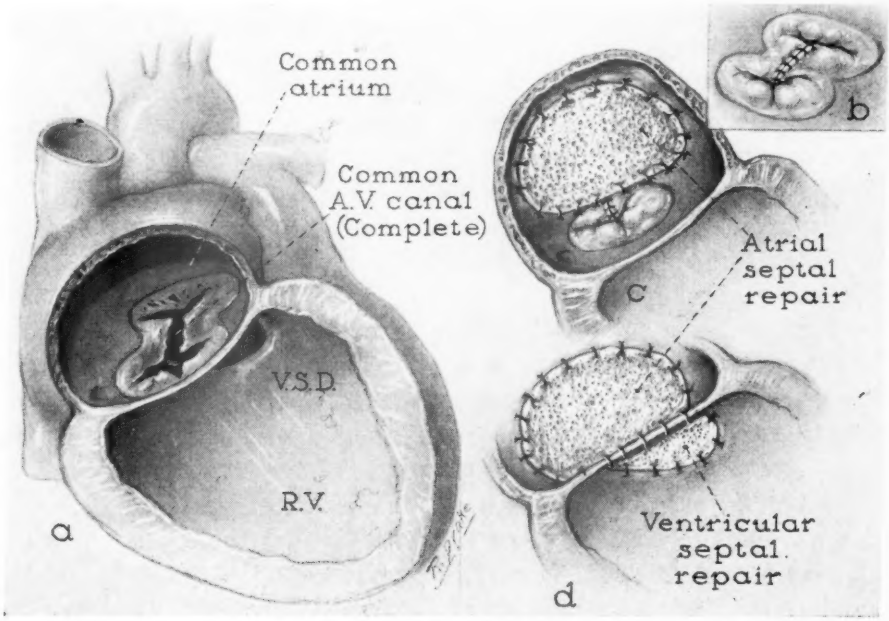

Fig. 2.—Common atrium. *A*, Lower portion of defect, similar to that seen in the complete form of common atrioventricular canal. *B*, Suture of cleft in mitral and tricuspid valves. *C*, New atrial septum in place. *D*, Closure of both atrial and ventricular septal defects.

Only rare reports of this condition are to be found in the literature. The clearest description with which we are familiar is by Cunningham.[3] In his case, which involved a 51-year-old man, the atrioventricular valves had the deformity characteristic of the complete variety of persistent common atrioventricular canal. The membranous part of the ventricular septum was absent; part of the inferior edge of the defect was comprised of a portion of the crest of the muscular ventricular septum which lay beneath the free edges of the common anterior and posterior atrioventricular leaflets, and the remainder of the inferior edge was formed by the atrioventricular valves.

Despite the absence of the membranous interventricular septum, interventricular communication did not exist, since the under surfaces of the atrioventricular valvular tissue were fused with the superior aspect of the muscular ventricular septum.

The case of Probyn-Williams,[9] which involved a newborn infant with pulmonary valvular atresia, was similar to that of Cunningham in respect to the atrial septum and the atrioventricular valves, as judged from the description. The drawing which accompanies the article, although not perfectly clear, suggests the presence of two intact atrioventricular valves.

In the case (No. 12) of Hart,[5] the specimen from a 2-year-old child was similar to that described by Cunningham, but failure of the common atrioventricular valve to join the ventricular septum had allowed free interventricular communication.

In the case (No. 3) of Gunn and Dieckmann,[4] which involved a 2-month-old boy, the atrial septum was represented only by a low muscular fold which extended from the left side of the ostium of the coronary sinus to the lower margin of the atrial defect. The membranous ventricular septum was completely formed. Although the mitral valve was normal, the septal cusp of the tricuspid valve was deficient (cleft) in its anterior third.

Zadoc-Kahn and Cousin[16] described the specimen from a 31-year-old man as having a single atrium with only a rudiment of an atrial septum in the posterosuperior aspect of the atrial chamber. An aneurysm of the membranous septum was present. The atrioventricular valves were not described.

In view of the current large number of operations performed to repair atrial septal defects, it is surprising that more cases of common atrium have not been reported. In reviewing a series of 63 repairs of atrial septal defect with use of hypothermia, Lewis and associates[7] referred to one possible instance of this type, using the term "continuous defect" to describe the condition. Watkins and Gross[15] described two instances of "common atrium" among 43 patients with atrial septal defect operated upon by closed technique. None of these 3 cases was reported as demonstrating anomalies of the atrioventricular valves.

There are two possible explanations for absence of the atrial septum. The simpler—but not necessarily the correct one—is that the septum primum and septum secundum, the elements that normally form the atrial septum, simply failed to develop. The other explanation is that the elements of the atrial septum may have formed normally but either the atrioventricular endocardial cushions failed to grow adequately or cushion tissue failed to unite with contiguous tissue.

The opinion has been given previously that septal defects within the heart are not necessarily results of deficiency of tissue.[13] Two elements which normally come together in the early stages of cardiac formation may not fuse normally even though present. Thus, if the two endocardial cushions which normally join the septum primum and septum secundum to complete the formation of the atrial septum should fail to fuse with the septal elements despite adequate growth, the elements of the atrial septum would not be fixed to the cardiac skeleton. With progressive growth of the heart, the inevitable tensions on septal tissue would be responsible for a progressively greater defect between the elements of the atrial septum and the endocardial cushions. The ultimate result would be either complete absence of atrial septal tissue or the presence of only a rudiment of septal tissue attached to the wall of the common atrium.

In the cases of absence of the atrial septum with which we are familiar, there was a strong tendency toward deficiency in the formation of the atrioventricular valves. This evidence strongly indicates that the basis for absence of the atrial septum is somehow accounted for by an abnormality of the development of atrioventricular valvular tissue. This abnormality may be in the amount of tissue formed, so that the cushions do not join the atrial septum, or it may represent failure in the process of fusion between cushion and septal tissue.

DIAGNOSIS

Clinical Features (Table I).—While there was some variation in the severity of symptoms among our patients of common atrium, 4 of the 5 had clinical features resembling those in the partial form of common atrioventricular canal.[1] In the fifth case the symptoms were more severe and resembled those usually associated with the complete form of common atrioventricular canal accompanied

TABLE I. CLINICAL FEATURES OF COMMON ATRIUM

CASE	1	2	3	4	5
Age	31	6	3	18	10
Symptoms					
Fatigue	+	+	+	+	+++
Cyanosis	-	+	+	+	++
Dyspnea	+	-	+	+	++
Physical findings					
Systolic murmur					
Pulmonary	+	++	++	++	++
Apical	++	+	+++	+	+
Diastolic murmur					
Apical	+	-	+	-	+
Second sound, pulmonary					
Split	-	+	+	+	+
Accentuated	-	+	+	+++	+++
Roentgenologic findings					
Cardiac enlargement	+	+	++	++	+++
Increased pulmonary vascularity	++	++	++	++	++
Electrocardiogram					
Right ventricular diastolic overload	+	+	+	+	+
Atrial enlargement	+	+	-	-	+

by severe pulmonary hypertension; and operation did indeed reveal a large ventricular septal defect in this patient. The other 4 patients had histories of slight but definite decrease in tolerance of exercise, easy fatigue, and shortness of breath following vigorous activity. Transient cyanosis with exertion was reported also. The fifth patient suffered from easy tiring and dyspnea, was cyanotic constantly, made a practice of squatting, and also evidenced failure of proper growth.

Cardiac auscultation in these 5 patients revealed many points of similarity. The cardiac impulse was right ventricular in character. A systolic murmur in the pulmonary region was noted in all cases and a different, slightly higher-pitched systolic murmur was detected at the apex with extension into the axilla. Apical diastolic murmurs were present in 3 of the patients. The second cardiac sound in the pulmonary region was abnormally widely split in 4 and markedly accentuated in 2 who had severe pulmonary hypertension.

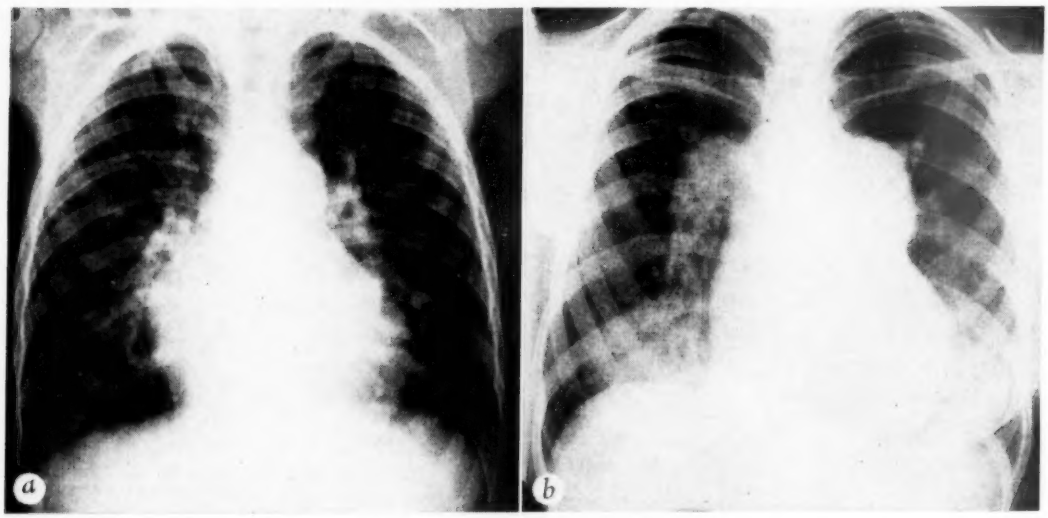

Fig. 3.—Posteroanterior views from Case 2 (*A*) and Case 4 (*B*) of partial form of common atrium.

Cardiac enlargement, as demonstrated by roentgenologic examination of the thorax, varied from slight to severe (Figs. 3 and 4). The apex was rounded and slightly raised from the diaphragm. The shadow of the pulmonary trunk was full or bulging on the left upper portion of the cardiac shadow and the right atrial bulge was prominent. Pulmonary vascular markings were increased moderately to severely in all patients.

The electrocardiograms were basically similar in these patients, and with regard to vectorial analysis of the QRS loops in the frontal plane they were identical to those described as characteristic of common atrioventricular canal defects.[12] These QRS vectors described a counterclockwise rotation with most of the loop lying superior to the isoelectric point (Fig. 5, *A*) or a figure-of-eight pattern located horizontally along the isoelectric plane with the initial loop rotating in a counterclockwise direction; the mean QRS axes

ranged from –60 to –150 degrees (Fig. 5, *B*). In all instances, precordial leads revealed variations of the rsR′ type of complexes in Lead V_1, interpreted as indicating diastolic overloading of the right ventricle. There was evidence of right ventricular hypertension in two cases, and patterns in the precordial leads suggested left ventricular overloading in two cases. P-wave changes indicating atrial enlargement were noted in 3 cases.

The diagnosis of common atrium is indicated clinically by the presence of the characteristic cardiac murmurs of atrial septal defect and mitral insufficiency associated with cardiac enlargement and roentgenologic evidence of increased pulmonary blood flow accompanied by definite cyanosis and the electrocardiographic features of common atrioventricular canal. Coexisting severe pulmonary hypertension does not alter these basic features but can be detected by the resulting accentuation of the second cardiac sound in the pulmonary region and the electrocardiographic evidence of right ventricular hypertension in addition to dilatation.

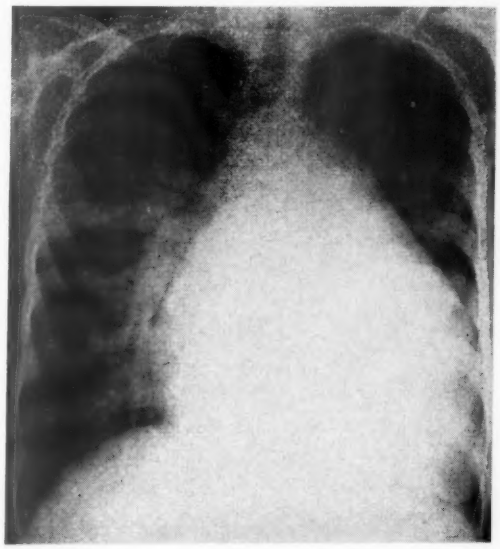

Fig. 4.—Posteroanterior view from Case 5, an example of complete form of common atrium.

Hemodynamic Features.—The hemodynamic diagnosis of common atrium depends upon the demonstration of complete mixing of the systemic venous return with the pulmonary venous blood. In the presence of common atrium, accurate comparison will demonstrate identical oxygen saturation in pulmonary artery blood and systemic artery blood. The functional term "total anomalous pulmonary venous drainage" has been used to designate this hemodynamic abnormality.[2, 11] As a condition resulting from common atrium this must be distinguished, however, from total anomalous pulmonary venous drainage resulting from other anatomic causes, which include anomalous connection of all of the pulmonary veins to the innominate vein, to the right atrium, to the superior vena cava, or to the inferior vena cava. In total anomalous pulmonary venous drainage associated with anomalous connection of all the pulmonary veins to the superior vena cava or a tributary thereof, it is usual to demonstrate that

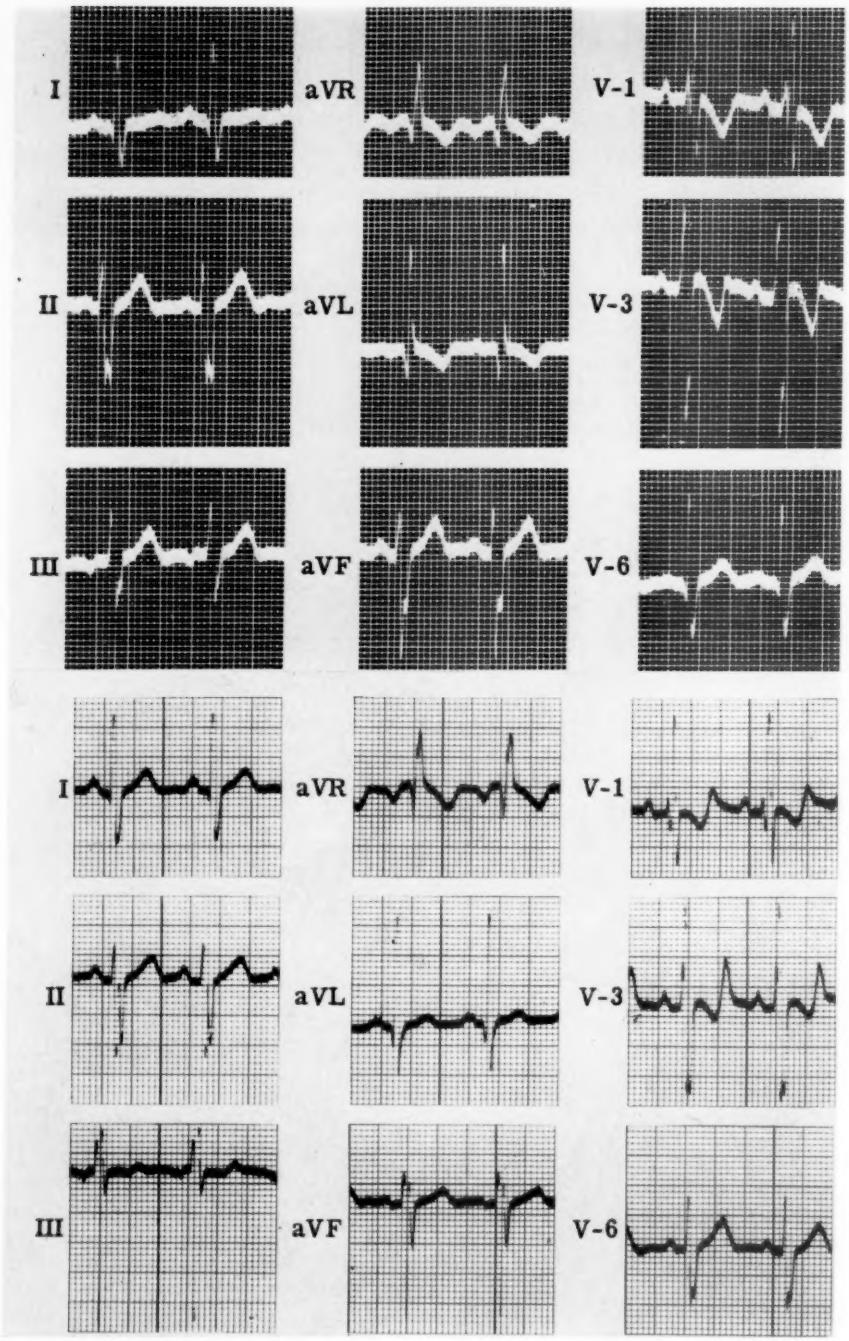

Fig. 5.—Electrocardiograms illustrating the two basic configurations encountered in cases of common atrium, also typical of common atrioventricular canal. Complexes of rsR′ type are noted in Leads V_1, interpreted as indicating diastolic overloading of the right ventricle, whereas left axis deviation is demonstrated by the standard leads. *A*, From a 3-year-old boy (Case 3). The QRS loop as projected in the frontal plane from the standard and unipolar extremity leads is described in a counterclockwise direction in the frontal plane, the major portion of the loop being located above the isoelectric point. Mean QRS axis is −110 degrees. *B*, From a 6-year-old boy (Case 2) with the other less common type of QRS loop which forms a figure-of-eight pattern located horizontally along the isoelectric line, the initial portion rotating in a counterclockwise direction. Mean QRS axis is −150 degrees.

oxygen saturation in blood of the pulmonary artery is higher by 1 to 3 percentage points than that of blood in the systemic artery because of preferential shunting of blood from the cavae.[10]

The position occupied by the catheter during catheterization is of aid in establishing the diagnosis of common atrium. When the tip of the catheter is made to enter the left ventricle, the shaft occupies an unusually low position in the cardiac silhouette, similar to that seen in common atrioventricular canal.[14]

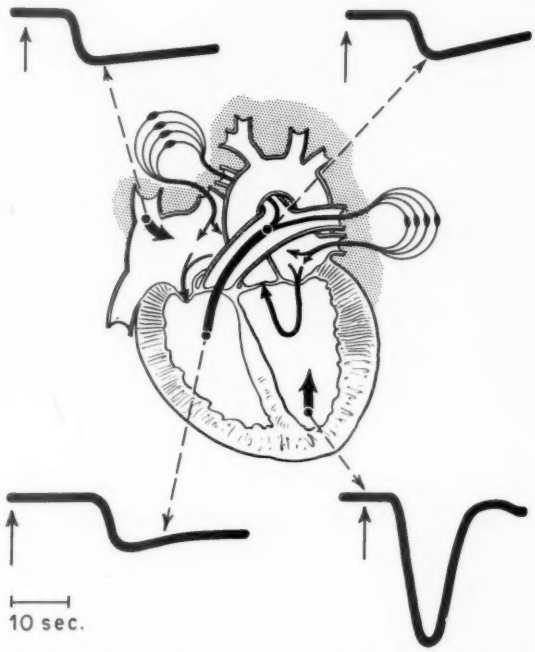

Fig. 6.—Diagrammatic representation of central circulation in total anomalous venous drainage associated with common atrium. Solid circles represent sites of injection of indicator and dilution curves inscribed in corners are those which would be recorded at a systemic artery. Downward deflections represent increasing concentrations of indicator, and vertical arrow shows instant of injection. Note similarity in contour of curves recorded from right side of heart, with shortest appearance time evident for superior caval curve.

Indicator dilution curves are of considerable value in the demonstration of common atrium. The principal features underlying their use are illustrated in diagrammatic form in Fig. 6. Briefly, indicator dilution curves obtained from patients with the functional condition of total anomalous pulmonary venous drainage associated with common atrium demonstrate identical contours after injection of dye into the pulmonary artery, the right ventricle, the right atrium, and the pulmonary veins. The diagnostic feature of these curves, however, is that the appearance time (interval between injection and first detection of dye at the sampling site) is greatest from the right ventricle and is least from the right atrium. This demonstrates that, while right ventricular blood must first traverse the pulmonary circulation, right atrial blood has ready access to the mitral valve. Dilution curves obtained with injection into the left ventricle are quite different, of course, and reflect the normality of the circulatory pathway from the left ventricle to the systemic circulation in the absence of a ventricular septal defect.

Three of the 5 patients were studied by the technique of right heart catheterization (Table II). The pulmonary artery pressure was elevated in Cases 3 and 4. The oxygen saturations of the pulmonary artery blood and the systemic artery blood were not found to differ by more than 1 per cent in any case. In all 3 patients the magnitude of pulmonary blood flow exceeded that of systemic blood flow, but total pulmonary resistance was elevated only in Cases 3 and 4.

TABLE II. PREOPERATIVE HEMODYNAMIC DATA FROM THREE CASES OF COMMON ATRIUM

CASE	1	3	4
Pressure (mm. Hg)			
Atrium	7/0	14/9	7/2
Pulmonary artery	15/5	60/32	115/65
Systemic artery	120/65	115/65	111/61
Oxygen saturation of blood (per cent)			
Mixed venous	69	59	68
Pulmonary artery	92	87	85
Systemic artery	92	87	85
Blood flow (L./min./m.^{2})			
Pulmonary	11.1	11.5	5.4
Systemic	3.0	4.2	3.2
Resistance (dynes sec. cm.$^{-5}$)			
Pulmonary	100	430	475
Systemic	1250	2000	1240

The oxygen saturation of systemic artery blood in the presence of functional anomalous pulmonary venous drainage is a function of the relative magnitudes of the pulmonary and systemic blood flows.[2] Thus patients with markedly increased pulmonary blood flow have a nearly normal systemic artery saturation of oxygen and clinical cyanosis may not be a feature in such cases. On exercise, however, since (presumably) the pulmonary flow either does not change or does not increase to the same degree as systemic blood flow, the systemic artery saturation of oxygen falls. This is evident from Table III, which records significant falls in oxygen saturation of blood in the 4 patients studied during exercise preoperatively.

TABLE III. ARTERIAL OXYGEN SATURATION IN COMMON ATRIUM AS DETERMINED BY EAR OXIMETRY DURING REST AND EXERCISE

CASE	1	2	4	5
Preoperative oxygen saturation (per cent)				
Rest	90	92	86	91
Exercise	85	90	75	87
Interval since operation (months)	25	15	9	Died
Postoperative oxygen saturation (per cent)				
Rest	97	95	91	—
Exercise	94	94	89	—

SURGICAL TECHNIQUES

Accurate, complete repair of the anatomic defect which characterizes the condition of common atrium requires the use of extracorporeal circulation. All

of the patients under consideration were operated upon in this manner, with use of a modified Gibbon-type vertical screen oxygenator.[6]

At operation the defect is carefully palpated with the finger inserted through the right atrial appendage. The presence of mitral insufficiency can be detected in this manner. It was present in varying degrees in all 5 patients. After extracorporeal circulation has been instituted, the right atrium is opened without arresting the heart. The anatomy of the defect then is evaluated fully.

The extent of the septal defect and the status of the lower edge of the defect are determined. If the lower end of the defect is formed by the fused mitral and tricuspid rings and only the mitral valve is cleft, the ventricular septum should be intact (Fig. 1, *A*). Under these circumstances the cleft in the mitral ring is repaired carefully with interrupted sutures of 5-0 silk (Fig. 1, *B*). Healing of such a suture line has been shown experimentally to be satisfactory.[8] A new atrial septum then is fashioned of partially compressed polyvinyl sponge (Ivalon) and is sutured in place with running 3-0 silk sutures interrupted at several points (Fig. 1, *C*). During placement of the stitches at the postero-inferior margin of the defect, care is taken to prevent injury to the cardiac conduction system. Four patients required repair of this type and all survived operation without heart block and made an uneventful postoperative recovery.

Patients 1, 2, and 3 are well 10, 20, and 25 months, respectively, after operation. Findings of postoperative oximetry carried out in two of them (Table III) were interpreted as within the range of normal, although in Case 1 the drop in oxygen saturation of the systemic artery blood with exercise was slightly more than might be expected. Patient 4 has shown clinical improvement, but cardiac catheterization carried out 8 months postoperatively revealed minimal residual right-to-left and left-to-right shunts and no drop in pulmonary artery pressure.

Patient 5 had a more complicated malformation, in which the lower edge of the atrial septal defect was identical to that seen in the complete form of common atrioventricular canal. Leaflets of both the mitral and the tricuspid valves were cleft, the ventricular septum had a defect below the common atrioventricular valves, and the mural leaflet of the mitral valve was fenestrated (Fig. 2, *A* and *B*). Repair of such a complex is difficult.

First the cleft valvular tissues are sutured as previously described so as to form two atrioventricular valves (Fig. 2, *B*). The cleft in the mitral valve usually requires more sutures than the one in the tricuspid valve. In the case under consideration, multiple interrupted sutures were required to close the fenestrations in the mural leaflet of the mitral valve.

Cardiac asystole is brought about by the injection of a 2.5 per cent solution of potassium citrate into the root of the aorta, and the right ventricle is opened. The ventricular septal defect extends anteriorly to the crista supraventricularis but may extend posteriorly for a considerable distance also. A semicircular, somewhat teardrop-shaped Ivalon prosthesis is sutured in place so that its base, or straighter edge, is attached to the under surface of the atrioventricular valvular tissue (Fig. 2, *D*). Interrupted mattress sutures sometimes have been helpful in carrying out this portion of such repairs.

Then the curved border of the prosthesis is sutured to the muscular border of the defect with running or interrupted silk sutures. The ventriculotomy incision is closed and the aortic clamp removed to allow resumption of cardiac action.

A new atrial septum then is inserted as previously described (Fig. 2, *C*). In effect, the lower end of this prosthesis is sutured to the ventricular prosthesis, a portion of the atrioventricular valvular tissue intervening between the two.

The patient with this complicated malformation failed to survive operation because of incomplete repair of the ventricular septal defect.

COMMENT

The anatomic malformation designated as common atrium probably is more common than has been appreciated heretofore. In the 3-year period during which open heart operations have been performed with use of extracorporeal circulation at the Mayo Clinic, 5 such cases have been encountered, whereas a brief review of the literature has revealed only 8 somewhat similar cases. It is possible that some cases of this type have been interpreted clinically as inoperable forms of atrial septal defect or common atrioventricular canal. With available methods, however, such an erroneous interpretation may be avoided.

In a case having clinical features of common atrioventricular canal, a finding of clinical cyanosis or desaturation of oxygen in systemic artery blood may be due either to increased pulmonary resistance and a predominant right-to-left shunt or to complete mixing of systemic and pulmonary venous blood in a common atrium. If the cyanosis is due to predominant right-to-left shunt, the condition is indeed inoperable at the present state of our knowledge. On the other hand, if it is due to complete mixing of systemic and pulmonary venous blood in a common atrium, not only is the condition operable but it may well be entirely curable.

The clinical and hemodynamic features which may alert the clinician to the diagnosis of common atrium have been detailed already. It should also be mentioned that patients with this malformation are prone to develop symptoms earlier in life than do most patients with the partial form of common atrioventricular canal and their symptoms usually are more pronounced.

How then can it be determined preoperatively whether or not a patient with a common atrium has a potentially curable lesion? It is important that operation be undertaken if pulmonary blood flow exceeds systemic flow. Since the systemic artery saturation in these cases is directly related to pulmonary and systemic blood flows, very low systemic artery saturation and marked cyanosis will be indicative of low pulmonary blood flow and suggestive of inoperability. Clinically, overactivity of the heart and radiologic evidence of enlargement of pulmonary arteries, not only at the hilus but in the periphery of the lung as well, are evidences of increased pulmonary blood flow. Electrocardiographic evidence of left ventricular diastolic overload, which is indicative of increased pulmonary blood flow in patients with uncomplicated ventricular septal defects, is not a reliable indication of operability in these patients. The presence of mitral insufficiency due to the cleft in the mitral

valve may lead to similar findings even in inoperable cases of common atrium. Recourse to cardiac catheterization is required for a final decision regarding operability in doubtful cases. The demonstration of pulmonary resistance in excess of systemic resistance suggests an inoperable condition.

SUMMARY

"Common atrium" designates a condition in which no atrial septal tissue, or virtually none, exists, and there is associated malformation of the atrioventricular valves. Five surgical cases are reported, in four of which there was a cleft in the septal leaflet of the mitral valve. In the fifth the tricuspid valve also was cleft, and the lower edge of the principal defect consisted of ventricular septum which itself was partially deficient.

Among the clinical findings in these cases were some of the features of common atrioventricular canal, and the hemodynamic findings resembled those seen in total anomalous pulmonary venous drainage. In such circumstances the clinical findings may be incorrectly interpreted as indicative of an inoperable form of common atrioventricular canal.

Extracorporeal circulation was employed in the operations performed in the 5 cases reported. One patient failed to survive operation. The 4 survivors are now well although pulmonary hypertension persists in one. Technical details of the methods for correcting this malformation are described.

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Discussion

DR. FRANK GERBODE (San Francisco, Calif.).—I sometimes think that maybe the noncompressed Ivalon is invaded more completely than the compressed. I would like to have you make a comment on this since you have had a good deal of experience with it.

DR. DENTON A. COOLEY (Houston, Texas).—Although Dr. Ellis may make reference to this in his manuscript, I would like to call attention to another intra-atrial lesion producing cyanosis. If the atrial defect is located close to the ostium of the inferior vena cava, blood from the cava may be preferentially shunted through the defect into the left atrium, as occurs in a patent foramen ovale in the fetus. The valvular mechanism of the cava and foramen ovale therefore produces a right-to-left shunt and cyanosis results.

The lesion under consideration Dr. Ellis referred to as "common atrium." We have used the term "common ventricle" in referring to a lesion in which there is an almost complete absence of the ventricular septum. It is important to distinguish this lesion from so-called "single ventricle" in which there is an associated rudimentary outlet chamber. In this latter lesion either the pulmonary artery, aorta, or both arise from the rudimentary chamber. Depending upon whether or not the atria are separated by well-developed atrial septum, the heart may be considered either trilocular or bilocular. The important consideration from a surgical standpoint is that common ventricle is a surgically correctible lesion whereas single ventricle is not as a rule.

Recently we have ceased using compressed Ivalon patches altogether in repair of septal defects of all types. In 2 patients the septal defect recurred more than a year after operation, and at a second operation a perforation occurred in the prosthesis itself. Accordingly, we now use patches of crimped knitted Dacron similar to the material in the aortic replacement grafts. The material is readily sutured into the defect and will not degenerate.

DR. ELLIS (closing).—I do not really believe it makes much difference what material is used to close the defect. Our initial laboratory experiences were concerned primarily with the noncompressed form of Ivalon. It is quite true, as Dr. Gerbode says, that tissues of the host grow into the noncompressed form of this material very readily. If the material is compressed too much, there may well be less chance of ingrowth. The way we have been using it, this has not appeared to be a problem. The condition to which Dr. Cooley referred is certainly a good example of an operable condition where cyanosis is present. One must determine in all of these patients, before considering them inoperable, whether or not the pulmonary flow is in excess of systemic flow. If this can be determined preoperatively, either from clinical evaluation of the patient or from catheterization studies, then the presence of desaturation per se is certainly no contraindication to operation.

ANASTOMOSIS BETWEEN THE SUPERIOR VENA CAVA AND THE RIGHT ATRIUM: A NEW TECHNIQUE AND A NEW APPLICATION

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INTRODUCTION

ANASTOMOSIS between the superior vena cava and the right atrium, first reported by Gerbode[3] in 1949, can be applied in a variety of pathologic conditions including malignant neoplasms of the mediastinum, chronic fibrosing mediastinitis, and aortic aneurysms. Recently, we have recognized its applicability to the surgical treatment of the anomalous venous drainage complicating some types of interatrial septal defects.

We consider the open method for the repair of atrial septal defects as the method of choice. It is entirely satisfactory for most defects, but difficulties may arise in repairing persistent ostium primum defects or high defects by the open or any other technique. In the event of a high defect, one or more right pulmonary veins enter the right atrium or the superior vena cava and they should be redirected into the left atrium before the actual closure of the defect is carried out. This may be done by placing a purse-string suture superior to the upper anomalous vein and then tying it down so as to guide the pulmonary veins to their proper termination in the left atrium. When this is obtained, as seen in Fig. 1, there may be narrowing of the anomalous pulmonary veins and the superior vena cava, with subsequent danger of thrombosis.[4]

We have encountered this complication in repairing high defects and have, therefore, been led to study the possibility of applying the atriocaval anastomosis to the surgical correction of the anomalous venous drainage. This can be done by performing an end-to-end anastomosis between the right auricle and the distal part of the superior vena cava and using the stump of the cava for redirecting the pulmonary veins into the left atrium. In doing this, the problem of narrowing of the anomalous pulmonary veins should be completely overcome. There will be no narrowing of the cava, if the anastomosis stays open, but this is the critical problem, because long-lasting patency of this anastomosis, as well as of all venous anastomoses, is difficult to achieve.

We have studied this problem in dogs and here describe an original technique that appears to be successful.

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METHODS AND MATERIALS

Healthy mongrel dogs weighing between 30 and 45 pounds were used, and the thoracotomy was done through the right third intercostal space. The superior vena cava was dissected free, and the pericardium was opened to expose the right atrium.

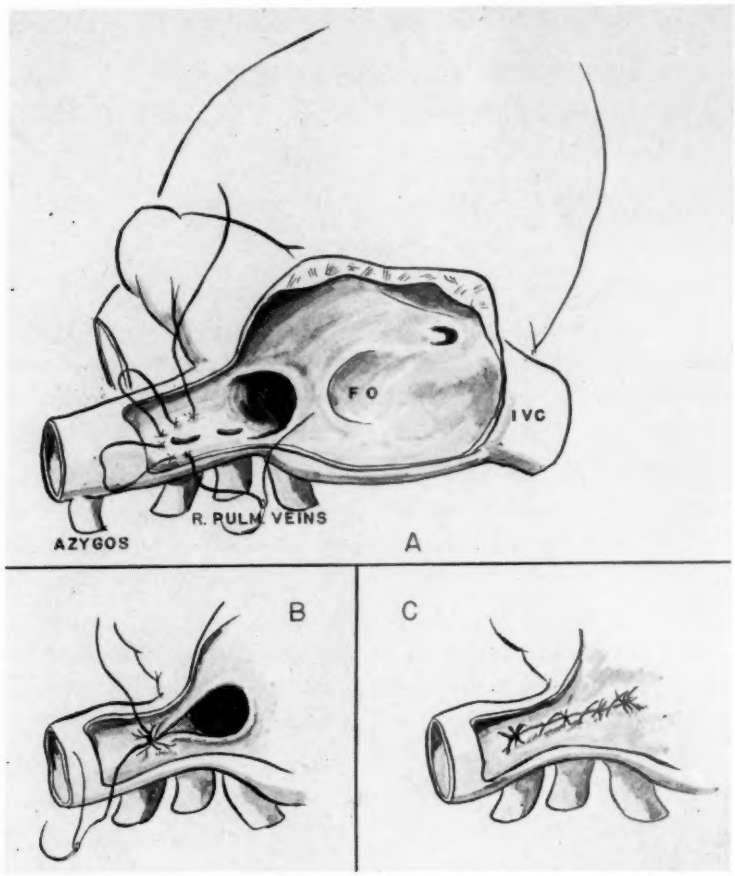

Fig. 1.—Narrowing of the anomalous pulmonary veins and superior vena cava, when the purse string is applied.

Fig. 2.—The plastic internal prosthesis used in Group B.

The superior vena cava was divided between two coarctation-type Potts clamps placed about 3 cm. above the azygos. The auricular appendage was then clamped at its base, and its tip was cut off. The clamp used on the atrium was a Potts coarctation type in some of the animals and a specially designed clamp in the others. The use of the Potts clamp was discontinued because a marked fibrotic reaction in the atrial tissue was noted in all the animals in which this clamp was employed. The atriocaval anastomosis was then carried out, using different techniques in the different groups of animals. In all instances, a 5-0 vascular silk with an atraumatic needle was used for the anastomosis. No heparin was given either locally or systemically.

No operative or immediately postoperative deaths were observed. In all animals, patency of anastomosis was determined by angiocardiography during life. Postmortem examinations were performed when the dogs were sacrificed or when they died. The 45 dogs used for this experiment were divided into three groups.

Group A (10 Animals).—In this group, a simple end-to-end anastomosis with continuous everting mattress-type sutures was performed. In all the animals of this group, a Potts clamp was used for clamping the auricular appendage. In the subsequent groups, a special clamp was employed.

Group B (8 Animals).—In this group, a rigid internal prothesis was used to perform the anastomosis. The prosthesis was made of Teflon (tetrafluora-ethylene) which is considered to be the least reactive plastic material available.[6] It had a highly polished inner surface and was shaped as shown in Fig. 2. This prosthesis was inserted; after that the lower row of sutures was applied and held in place by two temporary ligatures which were removed at the completion of the suture.

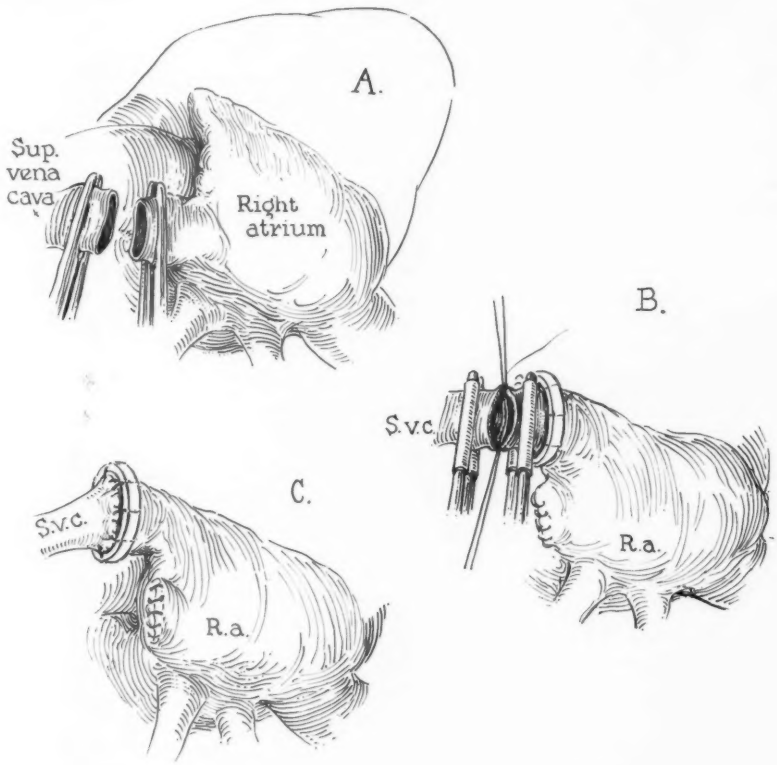

Fig. 3.—Schematic drawing of the anastomosis between superior vena cava and right atrium, with an external ring of support. *A*, The vena cava is divided between two clamps. *B*, The plastic ring is placed behind the caval clamp; the first row of suture is already in place. *C*, The anastomosis is completed, and the ring is sutured with interrupted stitches.

Group C (26 Animals).—In all the animals of this group, an end-to-end anastomosis with everting mattress sutures was performed, and an external ring support was applied. The ring has been made of Teflon, and it is provided with 8 holes that allow it to be anchored to the suture line.

Fig. 3 shows the technique of the use of such a ring. After the superior vena cava has been divided, the ring is placed behind the caval clamp, and, when the anastomosis is completed, it is attached to the suture line circumferentially by means of interrupted sutures. The sutures are placed in such a way as to catch both venous and atrial tissue.

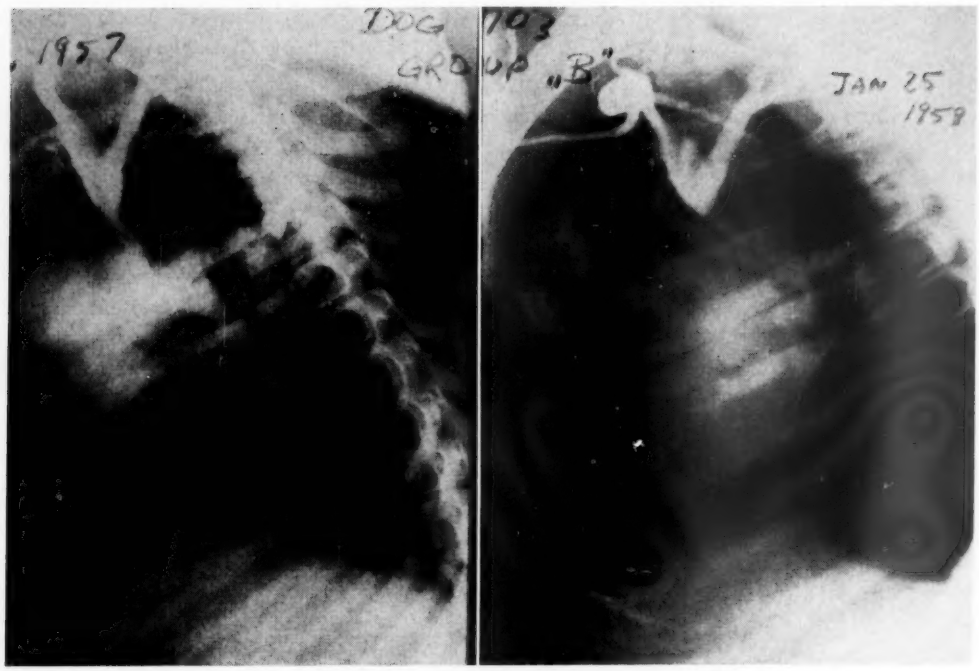

Fig. 4.—Serial venograms of an anastomosis of a dog of Group A. Note the gradual narrowing of the lumen.

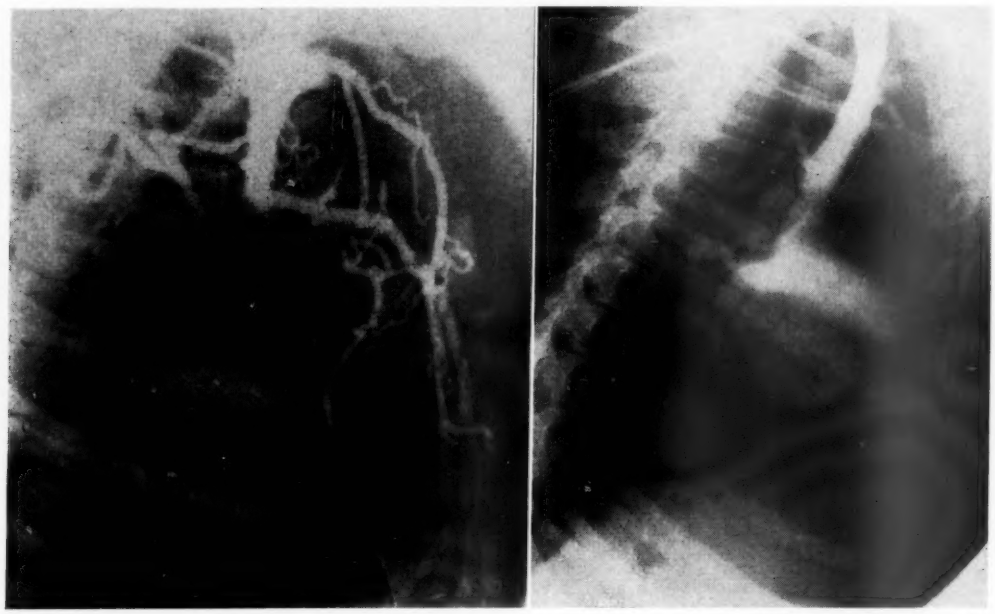

Fig. 5. Fig. 6.

Fig. 5.—Venogram of an anastomosis of a dog of Group B, showing complete occlusion, with development of collateral circulation.

Fig. 6.—Venogram of an anastomosis of a dog of Group C of one year's duration, showing full patency of the lumen.

RESULTS

Group A.—The simple end-to-end anastomosis resulted in a slow but progressive reduction of the lumen as followed by serial venograms in most of the animals (Fig. 4). This process led to a complete obliteration of the anastomosis in all but one dog in a period of time ranging from 2 to 22 weeks. Postmortem examination showed a severe fibrotic reaction around the suture line with subsequent thrombosis and complete obliteration of the lumen. Even in the dog with a patent lumen, there was an extreme narrowing.

Group B.—The use of an internal rigid prosthesis failed to keep the atriocaval anastomosis open. In fact, a rapid occlusion of the anastomosis, with development of an acute collateral circulation, was demonstrated by venograms in all cases (Fig. 5). Apparently this thrombotic occlusion occurred very early and was always observed when the first venogram was performed, as early as one week after the procedure. Postmortem examination showed a complete massive thrombosis of the lumen, with enormous dilatation of the superior vena cava. Intrapleural effusion was also observed in some animals.

Fig. 7.—Superior vena cava-to-right atrium anastomosis, with external ring of support, of one year's duration.

Group C.—The use of an external supporting ring was highly successful. In 24 of 26 animals, full patency of the anastomosis was observed at the time of postmortem examination, or when the last venogram was performed. This time ranged from 2 to 12 months after the procedure. Ten animals are still alive, and, in all, patency of the anastomosis has been demonstrated by recent venograms. Fig 6 shows a typical example of a venogram in one animal of this group.

Postmortem examination was done in the 16 animals that have been sacrificed or died, and there was full patency of the anastomosis without thrombus formation and with little or no fibrotic reaction in all but 2 animals. There was no constriction of the lumen in the 14 successful cases. Gross examination of the specimens showed the inner surface of the anastomosis to be perfectly smooth and apparently well endothelized (Fig. 7). This finding was confirmed by histologic examination performed in some instances.

In the 2 animals in which occlusion of the anastomosis was observed, a thrombus completely occluding the lumen was found. In one instance, the ring was found to be tilted and partially detached from the suture line with subsequent kinking of the superior vena cava. In the other case, no technical explanation of the failure can be offered.

DISCUSSION

The available data on venous anastomoses clearly indicate that long-lasting patency of the lumen is much more difficult to achieve than in the case of arterial anastomosis. This is particularly true when homografts or artificial prostheses are used. The results obtained with aortic homograft,[2] venous autografts, Ivalon, Dacron, and nylon tubes,[1] and silicone rubber tubes[5] have been uniformly disappointing. Gerbode[3] had some success, but our results have been poor; others have failed as well.

When a simple end-to-end anastomosis is used, the most probable cause of failure is the scar reaction along the suture line with contraction and secondary thrombosis leading to a total or subtotal obliteration of the lumen. In case of arterial anastomosis, the occluding force of scar tissue contraction is counterbalanced by the high intravascular pressure, which obviously is lacking in the case of a venous anastomosis. The results obtained in the first series of dogs are in general agreement with the data published to date on this subject. The results obtained with an internal plastic prosthesis, used in the attempt to combat the scar constriction observed in Group A, confirm the great likelihood of thrombosis when a foreign body is inserted into the venous blood stream. The plastic material we employed does not seem to be an exception to this rule.

The use of the special plastic supporting ring external to the anastomosis employed in Group C was the result of the experience gained with the two previous groups of experiments, and it is undoubtedly a rational approach to the problem of the scar contraction which tends to occlude the anastomosis during healing.

We feel that the results obtained with this technique are very encouraging. Furthermore, this method may be suitable, not only for the surgical treatment of the anomalous venous return, but for all cases where an anastomosis of the great veins is necessary.

SUMMARY

1. A simple end-to-end anastomosis between the superior vena cava and the right auricle failed in all but one dog to give a permanent patency of the anastomosis.

2. The use of an internal rigid prosthesis of Teflon resulted, in all the cases, in a rapid and complete occlusion of the anastomosis.

3. A special plastic supporting ring, external to the anastomosis, maintained a full patency for as long as one year of the atriocaval anastomosis in 24 of 26 dogs in which it was used.

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DISCUSSION

DR. THOMAS C. MOORE (Muncie, Ind.).—We, too, have been interested in this problem of atriocaval anastomosis. Dr. Riberi and I have published our experience relative to the use of an extension of Dr. Gerbode's original efforts in the field of atriocaval anastomosis. We have experienced a greater success with atriocaval anastomosis than has been reported here by Drs. Benvenuto and Lewis. A pedicle tube was created by us from the atrial appendage and atrium and the end of this pedicle tube was used for atriocaval anastomosis. In our series of 24 animals, we found that the anastomosis was patent in 23 of the 24 dogs at the time of cavogram or autopsy, up to 6 months after operation. When this study was submitted for publication 9 animals were still living. These animals were studied by cavogram only and were being saved for long-term observation. Since that time, we have carried out postmortem studies on 3 of these 9 animals, between 9 and 12 months following operation, and in all 3 animals, the atriocaval anastomosis and the pedicle tube of atrium and atrial appendage was as patent and free of thrombus formation as it had been in the animals previously autopsied and reported.

I should like to ask Dr. Benvenuto whether they ligate the azygos vein when they perform an atriocaval anastomosis.

DR. JOHANN L. EHRENHAFT (Iowa City, Iowa).—Last year at the meeting of the American Heart Association we reported on 4 patients upon whom the type of repair had been carried out as shown by Drs. Benvenuto and Lewis on experimental basis today. At the present time we have a total of 7 patients who have had correction of anomalous venous return from the right lung into the superior vena cava in association with interatrial septal defects. Partial anomalous venous return of the right pulmonary veins entering either the superior vena cava or inferior vena cava are frequently encountered during repair of interatrial septal defects. Sometimes the repair in those patients does present a serious problem, particularly in children in whom the superior vena cava may be of small size and in whom a modified atrioseptopexy with splitting of the superior vena cava to separate the superior vena caval blood stream from the pulmonary venous return is not feasible. The method outlined experimentally by the authors is very simple. Shunting of the pulmonary venous return through a modified atrioseptopexy through the interatrial septal defect into the left atrium is carried out. The superior vena cava is then transected and implanted into the tip of the right auricular appendage. We have not had any difficulties using this method clinically. All the procedures were carried out using hypothermia. There was no evidence of obstruction of the superior vena cava or thrombosis at the anastomosis site between superior vena cava and right auricular appendage. We do not believe that any prostheses or splints are necessary to prevent thrombosis or scarring at the anastomosis site at a later date.

DR. FRANK GERBODE (San Francisco, Calif.).—Some of you might be interested in our thoughts about this problem since we worked on it about 10 years ago. The last dog which I did in this series in 1950 was finally sacrificed on the altar of experimental surgery the other day and you might be interested in knowing that after 8½ years the patency in this particular instance of the inferior vena cava to the left atrium shunt was complete. In fact, you could hardly see where the anastomosis had been made.

There are a few things which are important in this type of anastomosis. First of all, the atrium, and most particularly the appendage does not like to be crushed, so if one is putting on a clamp to occlude it before doing a repair, it ought to be a very soft one. The Potts clamp is probably a very bad clamp for this purpose. We used a clamp made of two stiff wires closing just enough to bring the edges together. Also the anastomoses will be much more apt to stay patent if they are put in the thinnest portion of the atrium. The thicker the muscle to which the vein is anastomosed the more likely it is to fibrose and scar. This is probably a measure of the contraction of a thicker muscular wound and that is perhaps what has happened in some of these cases. An everting suture is also best.

DR. BENVENUTO (closing).—As to the question Dr. Moore asked, whether or not we did ligate the azygos, the answer is no, we did not ligate the azygos. I was aware of his good results, and as he pointed out, I had the impression that the tension is the crucial problem with this type of anastomosis. With his technique he does not have any tension while with just a simple anastomosis there is some tension. In our experiment we purposely cut off about 2 cm. of vena cava in order to have tension and in order to repeat as much as possible the clinical condition. This tension is very important in determining the occlusion of the anastomosis.

As far as the use of the Potts clamps is concerned, I do agree with Dr. Gerbode. It is an improper instrument for the auricular appendage. We noticed in the first group of animals in which we used Potts' clamps on the auricular appendage that there was a sort of constriction, a diaphragm-shaped constriction, in the auricular tissue. For this reason in the next two groups of animals we did not use this clamp but rather a specially designed clamp. I would like to show this clamp with the last slide.

This is the clamp we used. It is obviously a homemade one. The essential part is the tip of the clamp which is covered by some sort of plastic material which is not compressible but is still soft enough to avoid trauma to the auricular tissue.

Erratum

In the article by Arthur A. Michele, M.D., entitled "The Flip Sign in Sciatic Nerve Tension" in the November, 1958, issue of the JOURNAL, the illustrations marked Fig. 2 and Fig. 3 should be interchanged.